"THE ROLE OF CA19-9 IN PREDICTING TUMOR RESECTABILITY IN CARCINOMA OF THE HEAD OF PANCREAS "

A Dissertation Submitted to

The Tamil Nadu Dr. M.G.R. Medical University,

In partial fulfillment of the regulations for the award of the Degree of

MASTER OF SURGERY (GENERAL SURGERY)

Branch I: M.S. (Gen Surg)

Department of General Surgery,

GOVERNMENT STANLEY MEDICAL COLLEGE & HOSPITAL,

Chennai – 600 001.

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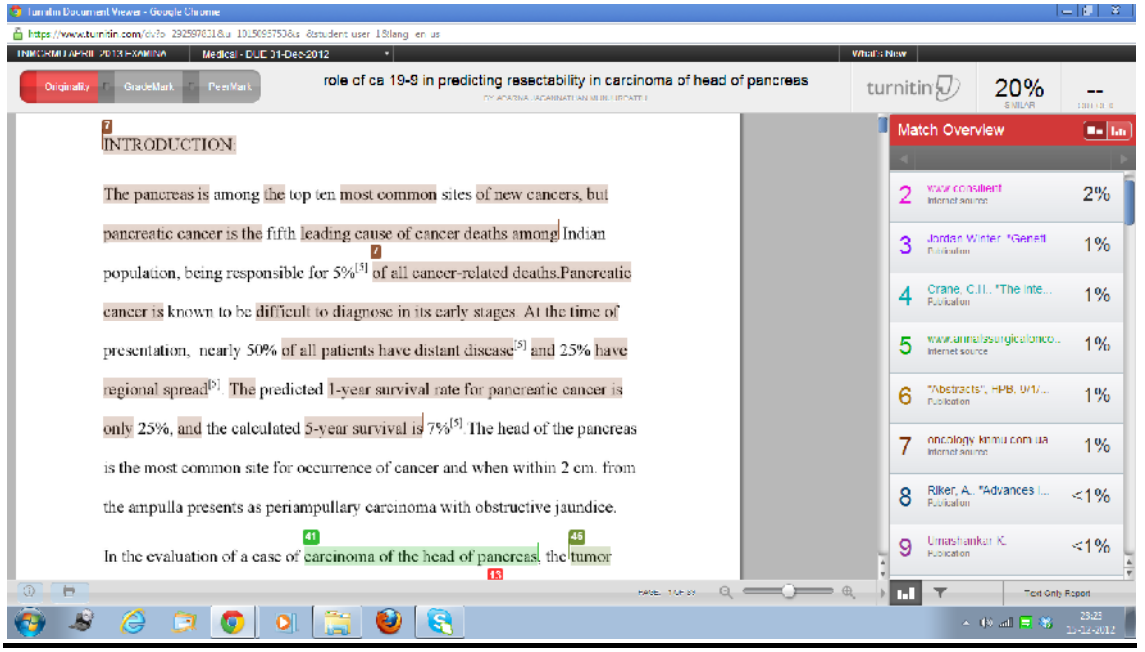
role of ca 19-9 in predicting resectability in carcinoma of head of pancreas
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INTRODUCTION
The pancreas is among the top ten most common sites of new cancers, but pancreatic cancer is the fifth leading cause of cancer deaths among Indian population, being responsible for 5%[5] of all cancer-related deaths.Pancreatic cancer is known to be difficult to diagnose in its early stages. At the time of presentation, nearly 50% of all patients have distant disease[5] and 25% have regional spread[5]. The predicted 1-year survival rate for pancreatic cancer is only 25%, and the calculated 5-year survival is 7%[5]. The head of the pancreas is the most common site for occurrence of cancer and when within 2 cm. from the ampulla presents as periampullary carcinoma with obstructive jaundice.
In the evaluation of a case of carcinoma of the head of pancreas, the tumor

INSTITUTIONAL ETHICAL COMMITTEE, STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work	: Role of CA 19-9 in predicting Tumour respectibidity In cancer Head of Pancreas
Principal Investigator	: Dr. M.J. Aparna
Designation	: PG in MS(Gen.Sur)
Department	: Department of Gen. Sur Government Stanley Medical College, Chennai-1

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 06.03.2012 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

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2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

MEMBER SECRETARY,
IEC, SMC, CHENNAI

CERTIFICATE

This is to certify that Dr. APARNA .M .J , postgraduate student (May 2010 – April 2013) in the department of General Surgery, Stanley medical college, Chennai, has completed his dissertation titled "**THE ROLE OF CA19-9 IN PREDICTING TUMOR RESECTABILITY IN CARCINOMA OF THE HEAD OF PANCREAS "** under the direct guidance and supervision in partial fulfillment of the regulations laid down by the Tamilnadu Dr.M.G.R. Medical University, Chennai for M.S., Branch – I General surgery degree examination

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DECLARATION

I, Dr.APARNA.M.J, solemnly declare that the dissertation titled "THE ROLE OF CA 19-9 **IN PREDICTING TUMOR RESECTABILITY IN CARCINOMA OF THE HEAD OF PANCREAS"** is a bonafide work done by me at Govt. Stanley Medical College and Hospital under the guidance and supervision of my unit chief,

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This dissertation is submitted to the Tamilnadu Dr. M.G.R. MEDICAL UNIVERSITY towards the partial fulfillment of the requirements for M.S., Branch I General Surgery degree examination.

Place: Chennai – 600001

Date: Dr. APARNA .M .J

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CONTENTS

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INTRODUCTION:

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Cancer antigen 19-9 (CA 19-9) is a tumor-associated mucin glycoprotein antigen that is related to the Lewis blood group protein[37]. This antigen is present in epithelial tissues of the pancreas, biliary ductular cells, stomach, gall bladder, colon, endometrium, salivary glands, and prostate[29]. Normal pancreatic juice, bile (in benign conditions), and even seminal fluid contain CA 19-9[18]. Blood levels may be elevated in healthy patients as well as in patients with benign and malignant conditions[6] .Its sensitivity (68-93%) and specificity (76-100%)[43] are inadequate for accurate diagnosis.Nonetheless when a diagnosis is made, it can be used to predict the extent of the disease and outcome after surgical resection.

REVIEW OF LITERATURE

BRIEF HISTORY:

Heterophilus,a Greek surgeon first described pancreas.

Wirsung identified the pancreatic duct in 1642.

Pancreas as a secretory gland was described by Graaf in 1671.

Morgagni 1769 first described pancreatic adenocarcinoma.

Kausch first two stage pancreaticoduodenectomy in 1912.

Brunschwig did the first radical pancreaticodudenectomy in 1937.

The first pancreatico-duodenectomy was done in one stage by Whipple in 1940.

ANATOMY:

GROSS ANATOMY:

The pancreas is a soft, yellow, glandular structure measuring approximately 20 cm in length and weighs about 95 g.It lies posterior to the stomach at the level of the second lumbar vertebra[13]. The organ is covered by peritoneum anteriorly, where it forms the floor of the lesser sac, and it is partially fixed to the retroperitoneum posteriorly. The retroperitoneal nature of the pancreas and its central position in the middle of the major abdominal blood vessels create some complicated anatomic relationships, as well as challenging surgical exposure. The pancreas also

has an intimate relationship with the second portion[18] of the duodenum, in which the two organs share a common blood supply, which makes their surgical separation generally impractical.

ANATOMIC DIVISIONS:

HEAD:

The head is the largest component of the pancreas, and it is located in the C loop of the duodenum[28] .The anterosuperior portion of the head is bordered by the antrum of the stomach and the first portion of the duodenum. The right lateral portion is bounded by the second part of the duodenum, and the left lateral extent ends at the neck of the pancreas. The inferior border is bounded by the third portion of the duodenum. The flat anterior surface forms the posterior extent of the lesser sac with a bare area intervening where the omental bursa of the transverse colon is attached[28] . These peritoneal layers contain middle colic artery, which arises from the superior mesenteric artery.[19]

UNCINATE PROCESS:

The uncinate process of the pancreas is a continuation of the head, which arises from the original ventral pancreatic bud[19]. It lies

posteromedial to the head.It is variable in size and position, and it is interposed between major vascular structures in two different planes. It separates the inferior vena cava and the portal vein in the dorsoventral plane[8] . The aorta and the superior mesenteric artery are separated in the sagittal section. The uncinate process lies adjacent to the superior mesenteric artery, or it may completely encompass it[8]. An anomalous right hepatic artery which originates from the superior mesenteric artery may pass through it.

NECK:

The neck is the smallest part of the pancreas, and it is 1.5 to 2.5 cm long. It lies directly over the portal vein, that creates a groove over its posterior surface, as well as the superior mesenteric pedicle. Although generally lateral tributaries from the parenchyma of the neck to the superior mesenteric vein are present, anterior tributaries are rare. This allows an avascular plane to bedissected between the neck and the superior mesenteric-portal vein.. The neck is that portion of the pancreas that is usually divided during a pancreaticoduodenectomy for a lesion in the pancreatic head.

BODY:

The neck continues towards the left as the body of the pancreas, which begins lateral to the superior mesenteric artery. It is related superiorly to the splenic artery. Anteriorly, the body forms the floor of the lesser sac. The splenic vein forms a posterior relation to the body, where it is embedded in the pancreatic parenchyma. The inferior margin of the body provides an attachment of the transverse mesocolon to the posterior abdominal wall.

TAIL:

The body continues as the tail of pancreas which extends toward the splenic hilum. The tail is differentiated from therest of the pancreas by its mobility It usually lies within the lienorenal ligament. The position of the tail with respect to the hilum is not consistent, and it may reach the spleen in only 50% of individuals.

PANCREATIC DUCTS:

The ductal anatomy of the pancreas shows two named ducts: the main pancreatic duct (Wirsung) and the accessory pancreatic duct (Santorini)[20]. The main duct begins at the tail of the pancreas and runs close to the posterior surface of the pancreas,midway between the superior and inferior borders to reach the head[20] . Under normal circumstances, the diameters of the duct average 2.4, 3.5, and 4.8 mm in the tail, neck, and head, respectively. Approximately 18 to 20 tributaries enter the main duct at right angles along its course;[13] there also are additional inconsistent tributaries from the uncinate process. Once the duct passes over the superior mesenteric-portal vein confluence[16] in the neck of the pancreas it enters the head, and it takes a more posterior course to eventually join the common bile duct. Both finally end int the majordudenal papilla.

The anterosuperior portion of the pancreatic head is drained by the accessory pancreatic duct[9], which empties through the minor duodenal papilla (70%) or into the main pancreatic duct. The accessory duct has a demonstrable communication wit the main duct in the majority of patients.

AMPULLA OF VATER:

The ampulla of Vater is the dilated distal confluence of the pancreaticobiliary ductal system[46]. An ampulla exists only when the two ducts join far enough from the papilla. The greatest diameter of a normal duct is between 3 and 4.5 mm near its termination in the duodenum. The duct is tapering towards the tail.

DUODENAL PAPILLA:

The major papilla (the papilla of Vater) lies on the posteromedial wall of the second part of the duodenum[8] or, rarely, the third portion. The papilla usually lies 7 to 10 cm distal to the pylorus, approximately at the level of the L 2.

The minor papilla drains the accessory pancratic duct, and it usually lies 2 cm cranial to the major papilla. The minor papilla lies distal to the point where the gastroduodenal artery crosses behind the duodenum.

ARTERIAL SUPPLY:

The pancreas relies on a dual arterial blood arising from the celiac trunk and the superior mesenteric artery. [9]

The head of the pancreas, the uncinate process, and the C loop of the duodenum share an anastomosing blood supply. The gastroduodenal artery arises from the hepatic artery proper and gives off the superior pancreaticodudenal artery[36] which gives off anterior and posterior branches. They supply the head of the pancreas and the second portion of the duodenum. The inferior pancreaticoduodenal artery arises as the first tributary of the superior mesenteric artery [13] as it emerges from the lower border of the pancreas. These two vessels anastomose freely, and this makes it difficult to surgically separatethe two structures.The rest of the pancreas is also fed by a dual blood supply. The splenic artery,gives off its first major branch the dorsal pancreatic artery, near the inferior edge of the gland,this artery divides into two branches. One travels to the right and connects with the anterior superior pancreaticoduodenal artery. The other is the transverse pancreatic artery[13] , which runs towards the,nourishing the body and the rest of the tail.

VEINS:

The veins usually lying superficial to the arteries and parallel them. The veins srain into the superior and inferior mesenteric veins, the splenic vein, and finally into the portal system.[15]

The head and uncinate process of the pancreas have four pancreatoduodenal veins[15]. The anterior superior pancreatoduodenal vein drains into the right gastroepiploic vein, which is atributary of the superior mesenteric vein. The posterior superior pancreatoduodenal vein drains directly into the portal vein[9]. Both the inferior anterior and posterior pancreatoduodenal veins empty into the superior mesenteric vein. Tributaries seldom enter the superior mesenteric or portal vein from their anterior surface[15] .The body and tail of the pancreas is drained by the splenic vein,and the transverse pancreatic vein, which may empty into the superior mesenteric, inferior mesenteric, or, sometimes, splenic vein[19].

LYMPHATICS:

The lymphatic drainage pattern of the pancreas includes five routes of drainage.While the superior nodes arising from the anterior and posterior portions of the pancreas, drain into the lymph nodes on the superior surface of the pancreas[27] . the inferior collecting trunks terminate in lymph nodes along the inferior border.Anterior collecting trunks terminate in the infrapyloric and anterior pancreatoduodenal lymph node. The posterior surface, empties into the corresponding posterior lymph nodes. The lymphatics from the tail drain into splenic hilar lymph nodes.

NERVES:

The pancreas is innervated by both the sympathetic and parasympathetic nervous systems from the splanchnic and vagus nerves, respectively[9]. Efferent motor fibers innervating the ducts, acini, and blood vessels are provided by both divisions. In the sympathetic division, preganglionic fibers are provided from the greater and lesser splanchnic nerves, whereas the celiac plexus contains the efferent fibers from the pancreas.The parasympathetic nervous system primarily innervates the pancreas via the celiac branch of the posterior or right vagus.

HISTOLOGY:

Pancreas consists of both exocrine and endocrine units termed *acini* and *islets of Langerhans*, respectively. The acinar cells are arranged in rounded structures and are pyramidal. These cells contain zymogen granules and the cell bodies of the postganglionic parasympathetic neurons are interspersed between the acinar cells. The pancreatic acinar and duct system secretes about 1 L of fluid per day that is rich in digestive enzymes, sodium, and bicarbonate.

The islets of Langerhans constitute 1 to 2% of the pancreatic massThe various hormones secreted in the pancreas are insulin,glucagon,somatostatin,pancreatic polypepetide.

EMBRYOLOGY:

The pancreas is formed from two separate buds arising from the endodermal lining of the duodenum. The ventral bud appears first at about the third week. The ventral bud forms the uncinate process and the lower part of the head of the pancreas[22] . The remainder of the gland usually arises from the dorsal bud. The main pancreatic duct arises by the fusion of the ductal components . Failure of fusion occurs 10% of the time, causing a persistent double duct system known as pancreas divisum. This rarely causes pancreatitis.

The islets of Langerhans arise in the pancreatic parenchyma during the third month of life. These islands of cells are present throughout the gland. Insulin secretion begins roughly at the fifth month.

INCIDENCE:

Adenocarcinoma of the pancreas remains a relatively incurable disease despite advances in surgical care of the resected patient, the move toward enrolling patients in clinical trials, and advances in systemic treatment for other solid tumors of the gastrointestinal tract. Characteristically, patients present late in their disease with minimal vague symptoms. The combination of aggressive tumor biology and ineffective therapies usually results in the rapid decline of these patients, resulting in death within a few months after diagnosis. Survival from this disease is poor with approximately 23% of patients alive 12 months following diagnosis and 5% alive at 5 years[34]. Men are more commonly affected than women,mortality rates range from 7 to 9 per 100,000 for men and 4.5 to 6 per 100,000 for women[42] .It is a disease of the elderly. Only 10% of patients present before the age of 50, while those aged 50 to 54 experience an incidence of 9.8 per 100,000, and those 70 to 74 an incidence of 57 per 100,000. The median age of diagnosis with pancreatic cancer is 72, with less than 13% of cancers diagnosed prior to the age of 55 and greater than 69% of cancers diagnosed after the age of 65.

GENETICS OF PANCREATIC MALIGNANCIES:

Four categories of mutated genes play a role in the pancreatic tumorigenesis: oncogenes, tumor-suppressor genes, genome-maintenance genes, and tissue maintenance genes[40]. Some of these mutations are germline but those genetic mutations acquired during life, termed somatic mutations, contribute to tumorigenesis within a tissue but are not passed to offspring.

TUMOR SUPPRESSOR GENES:

Tumor suppressor genes are mainly involved in regulating the cell cycle and blocking uncontrolled cell proliferation. Deletion, mutation, chromosomal rearrangements are methods by which genetic alterations can occur and hence result in an unregulated cell cycle. At least genes in this group are known to be involved in the development of pancreatic cancer, they include[1]

p16

p53

DPC4

BRCA2

MKK4.

ONCOGENES:

Oncogenes are products of precursor proteins known as proto oncogenes which get activated by mutation.Most commonly involved genes are

K-RAS

BRAF

DNA MISMATCH REPAIR GENES:

DNA mismatch repair genes code for protein products which make amends for the various discrepancies that would take place when DNA is replicating[1]. When these repair genes are rendered mutant, flaws encountered in DNA sequences are left unrepaired. One such example is in the case of RER+ (replication error-positive) tumors.[40]

GROWTH FACTORS:

Contributory evidence exixts to suggest that the increased expression of some of the peptide growth factors play a significant part in the initiation and biological behaviour of the tumor. These factors can act either in an autocrine or paracrine fashion.The important ones are:[1]

EGFR

TGF-beta

FGF

IGF

EPIDEMIOLOGY AND RISK FACTORS:

Adenocarcinoma is the most common malignancy of the pancreas.It forms more than three fourths of all tumors of the pancreas.[12]

DEMOGRAPHIC FACTORS:

- ✓ Increasing age is an important risk factor for pancreatic cancer, with more than four fifths of the cases occurring in patients in the 60-80 years age group.[16]
- ✓ The gender distribution of pancreatic cancer is not particularly remarkable,but males are more commonly affected by the disease.
- ✓ The risk is increased among the black population and is around 3 times higher than in the white population.

HOST FACTORS:

The most important host factors are the six genetic syndromes. These syndromes are:[1]

- ✓ hereditary nonpolyposis colorectal cancer (HNPCC)
- ✓ familial breast cancer associated with *BRCA-2* mutations
- ✓ Peutz-Jeghers syndrome
- ✓ ataxia-telangiectasia syndrome
- ✓ familial atypical multiple mole-melanoma syndrome (FAMMM)
- ✓ hereditary pancreatitis.

Chronic pancreatitis, has been stated as an important risk factor for the development of pancreatic cancer . [5] There is enough evidence to suggest that when the diagnosis of chronic pancreatitis and pancreatic cancer are separated by an interval of less than 10 years,it might be an important risk factor . This might suggest that chronic pancreatitis is an early indicator of an undiagnosed occult pancreatic cancer.

The association between pancreatic cancer and diabetes is inconclusive. Studies have demonstrated that diabetes is an important risk factor only when the diagnosis precedes that of pancreatic cancer within 5 years and when patients are diagnosed after the age of 40 years. These data suggest that more than a causal association, recently diagnosed diabetes is an early symptom of pancreatic cancer.[1]

Other possible host factors that might have a role are thyroid tumors, other benign endocrine tumors, and cystic fibrosis.[1]

ENVIRONMENTAL FACTORS:

- ✓ Cigarette smoking
- ✓ Foods rich in carbohydrate,triglycerides,salted foods
- ✓ Alcohol
- ✓ coffee

PATHOLOGY:

Ductal adenocarcinoma, the most common primary pancreatic malignancy, accounts for approximately 80 % of all primary nonendocrine cancers. [1]The region wise incidence is:

65% -head,neck,uncinate process

15%-body and tail

20%-diffusely distributed throughout pancreas

On cut section, adenocarcinomas are whitish ,poorly demarcated lesions that often cause stricturous narrowing of the distal common bile duct.[19]

Because of the intense infiltrative nature, identifying the exact size of the tumor intraoperatively is seldom possible. Microscopic analysis often shows that the tumor often extends outside of the grossly demarcated mass. On histologic analysis, infiltrative glandular components surrounded by a severe fibrotic reaction are noticed. The epithelial cells often contain mucin and are thrown into multiple papillary and cribriform structures. These tumors characteristically demonstrate lymphovascular, perineural invasion and this might suggest a poor outcome.

Adenocarcinomas, are rapidly growing tumors; most tumors that are removed would have already spread through the lymphatics to regional lymph nodes. In addition, these tumors directly infiltrate the various adjacent intraperitoneal and retroperitoneal structures . At the time of death, up to four fifths of them have metastatic lesions in the liver,three fifths have peritoneal implants, nearly half of them have lesions in the lungs or pleura, and one fourth have deposits in the adrenal glands.

Adenosquamous is a variant with mixed contributions from both histological varieties. It is common among patients who have received chemotherapy+ radiation and has tumor properties similar to adenocarcinoma.

SYMPTOMS AND SIGNS:

The clinical presentation of pancreatic cancer depends on the location of the tumor within the gland, with most symptoms initially appearing vague and nonspecific.The majority of pancreatic tumors develop in the region of the head, subjecting the pancreatic portion of the bile duct to occlusion .[8] Jaundice is, therefore, the first presenting symptom and may be associated with pruritus, clay coloured stools and high coloured urine.It may have been associated with previous episodes of biliary colic, anorexia, or vague gastrointestinal distress. Patients with pancreatic cancer initially develop a vague epigastric pain radiating to the left subscapular region.Loss of weight, appetite, other systemic manifestations like anorexia, myasthenia, and alternating constipation and diarhhoea are seen in many patients. Nausea and vomiting,indicate early gastric outlet/duodenal obstruction and may be a sign of locally advanced disease.

Some tumors of the pancreatic head or body will not involve the bile duct but may invade the duodenum or neural structures, including the celiac or mesenteric plexi. Such invasion results in pain that may be characterized by aching, pressure, or burning. Tumors in the head of the pancreas, located off the midline to the right, may lead to pain in the right

upper quadrant or epigastric area. Tumors involving the pancreatic body usually lead to midepigastric pain, and those in the tail often cause left-sided abdominal pain. Back pain is more suggestive of infiltration of the retroperitoneum.

Pancreatic exocrine insufficiency manifested by steatorrhea occurs relatively infrequently as a presenting symptom, and while it is often initially mild and easily manageable, it may worsen after surgical resection or radiation therapy. Pancreatic ductal obstruction may lead to acute pancreatitis, which is occasionally a presenting sign of pancreatic cancer. When a patient without risk factors for pancreatitis experiences an acute attack, an underlying pancreatic cancer should be considered and thoroughly investigated. Importantly, it is increasingly recognized that glucose intolerance or overt diabetes is found in up to 70% of patients, and when diabetes develops in an older adult or when it is found in conjunction with other symptoms such as pain, anorexia, or weight loss, the possibility of an underlying pancreatic neoplasm should be raised.[33]
Other symptoms of pancreatic cancer include superficial or deep venous thromboses, anorexia, or weight loss. In some studies, weight loss is the most common symptom of pancreatic cancer. Unfortunately, initial symptomatology, to include weight loss, may be indicative of metastatic

disease, such as night sweats, significant fatigue, or liver pain. Gastric outlet obstruction, increasing abdominal girth from ascites, and skin manifestations all occur in pancreatic cancer, but are fairly uncommon as presenting signs and symptoms.

Patients with pancreatic cancer usually have an unremarkable physical examination, but the most common abnormal physical finding is jaundice, which may be accompanied by cutaneous excoriations related to pruritus. In patients with advanced disease, temporal muscle wasting, hepatomegaly or a nodular liver, left supraclavicular lymphaadenopathy (Virchow's node), deposits around the umblicus (Sister Mary Joseph's nodules), or the unusual finding of metastasis at Blumer's shelf may be discovered on digital rectal examination.[1]

PROGRESSION OF PANCREATIC CANCER:

Pancreatic ductal adenocarcinoma arises from ductal epithelial cells. Neoplasia arising from these cells progress from initial intraductal proliferative lesions to invasive carcinomas similar to other carcinomas from ductal epithelium, such as breast ductal carcinoma or prostate cancer. Pancreatic intraepithelial neoplasm (PanIN) is the term established for intraductal proliferative epithelial lesions. This replaces old nomenclature such as metaplasia, dysplasia, hyperplasia, and carcinoma in situ. PanINs

are graded as 1A, 1B, 2, and 3 as they advance along a histologic continuum of progressive dysplasia.The evidence that these lesions are precancerous include the observation that following segmental resection of pancreata with PanINs in the resected tissue, pancreatic cancer can develop in the pancreatic remnant.

STAGING:[3]

PRIMARY TUMOR (T)

TXPrimary tumor cannot be assessed

T0 No evidence of primary tumor

TisCarcinoma *in situ* (also PanIN 3)

T1 Tumor limited to pancreas, 2 cm or less in greatest dimension

T2 Tumor limited to pancreas, more than 2 cm in greatest dimension

T3 Tumor extends beyond the pancreas but without involvement of the celiac axis or the superior mesenteric artery

T4 Tumor involves the celiac axis or the superior mesenteric artery (unresectable primary tumor)

REGIONAL LYMPH NODES (N)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis

DISTANT METASTASIS (M)

MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

STAGE GROUPING

Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
Stage IIA	T3	N0	M0
Stage IIB	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage III	T4	Any N	M0
Stage IV	Any T	Any N	M1

Another staging system has been proposed by the Japan Pancreas Society (Table-1), including other factors such as serosal invasion (S factor), retroperitoneal invasion (RP factor), and portal vein invasion (PV factor).

Table 1 -- Japan Pancreas Society Stage Classification [2]

Stage Grouping	**T**	**S**	**RP**	**PV**	**N**	**M**	**5-Yr Survival**
Stage I	T_1	S_0	RP_0	PV_0	N_0	M_0	35–45%
Stage II	T_2	S_1	RP_1	PV_1	N_1	M_0	15–25%
Stage III	T_3	S_2	RP_2	PV_2	N_2	M_0	5–15%
Stage IV	T_4	S_3	RP_3	PV_3	N_3	M_1	0–10%

Tumor (T)
T_1 = 0 to 2 cm
T_2 = 2.1 to 4 cm
T_3 = 4.1 to 6 cm
T_4 = >6.1 cm
Serosal invasion (S); Retroperitoneal invasion (RP); Portal venous invasion (PV)
0 = Absence of invasion

1 = Suspected invasion
2 = Definite invasion
3 = Severe invasion
Lymph nodes (N)
N_0 = No metastasis
N_1 = Primary lymph node group metastasis
N_2 = Secondary lymph node group metastasis
N_3 = Tertiary lymph node group metastasis
Distant metastasis (M)
M_0 = No distant metastasis
M_1 = Distant metastasis

INVESTIGATIONS:

SERUM BIOCHEMISTRY:

Serum total and direct bilirubin, ALP,GGT,5' nucleotidase values are raised.The levels of hepatic transaminases may be unremarkable or may be mildly elevated owing to acute liver injury. Coagulation profile may be deranged due to hepatocellular dysfunction . Decreased enterohepatic

circulation results in malabsorption of fat-soluble vitamins A,D,E,K and subsequent defeciency of vitamin K-mediated coagulation products. Low albumin levels, normocytic anaemia are present.

IMAGING MODALITIES:

With advances in imaging modalities,the set goals for the use of various investigations are as follows:

(1) exploration can be limited to those patients with a high likelihood of resection,

(2) objective criteria can be utilized to assess resectability rather than subjective imprecise tactile perception,

(3) patients who will require venous reconstruction at time of resection can be identified, optimizing preoperative planning,

(4) patients may move on to neoadjuvant therapy appropriate for their stage of tumor without an initial exploration, and

(5) patients exhibiting an advanced tumor can be palliated with less morbid nonoperative procedures.

ULTRASONOGRAPHY:

Ultrasonography in pancreatic cancer, as in other diseases, is particularly operator dependent, and in experienced hands may safely replace assessment with helical CT.It is used as an initial creening image to localise the lesion in a case of obstructive jaundice.It remains the most important screening test to analyse the anatomical origin of the disease owing to its sensitivity in demonstrating a dilated biliary system in cases of obstructive jaundice. It also provides details regarding liver surface deposits, mass lesion, peripancreatic lymph nodes, free fluid, Ultrasound scans reveal a pancreatic mass in well over 50 % of patients with pancreatic cancer. Nevertheless, a negative scan does not definitively rule out pancreatic cancer.

Computerised Tomography(CT SCAN):

CT scanning is the most commonly used imaging modality for confirmation of the diagnosis and for staging. Standard CT scans are incapable of predicting the operability of the tumor. Nevertheless, major vessel infiltration and hepatic metastases can be best assessed with newer techniques. Currently,the standard is the multiphase CT scan, coordinating iv contrast with serial films in arterial, portal venous, and parenchymal phases .[4] This must be obtained on a helical CT scanner, allowing acquisition during a single breath-hold for each phase. With this type of

CT, extension of the tumor to the superior mesenteric artery (SMA), celiac axis, superior mesenteric vein/portal vein (SMV-PV) complex, and contiguous structures can be clearly determined as well as an assessment of distant metastasis.

Resectability is defined on multiphase CT by[4]

(1) the absence of extrapancreatic disease

(2) patency of the SMV-PVconfluence

(3) SMA abutment-involvement less than 180 degree.

Distortion of the fat plane between the mass and the SMV-PV identifies tumor invasion of the vein or fibrosis and defines the patient who may require a vein reconstruction at the time of resection.The accuracy of CT scan in predicting operability of a pancreatic cancer ranges from 80-90%.

Subcentimetric tumors can be missed, and a dilated biliary system may be the sole report on CT. This should raise the suspicion of malignancy and should be followed up by other investigations.

Optimally, CT imaging should precede stent placement and biopsy due the possibility of postprocedure inflammation from the biopsy and artifact from the stent that can confound interpretation of the images.

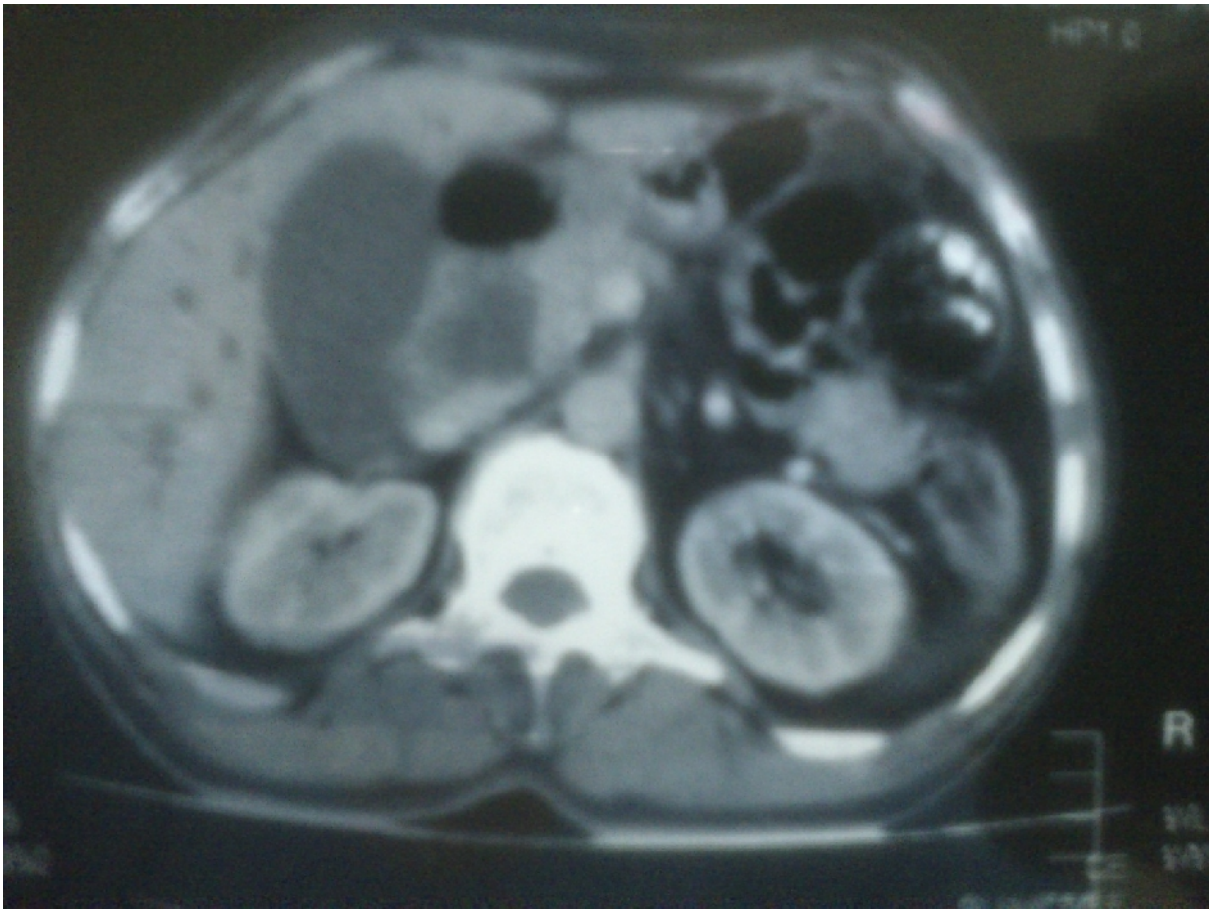


Fig.1-This a CT SCAN picture showing a hypodense lesion in the head of pancreas with distended Gall bladder,dilated biliary radicles,hypodense lesion in the liver suggesting metastasis.

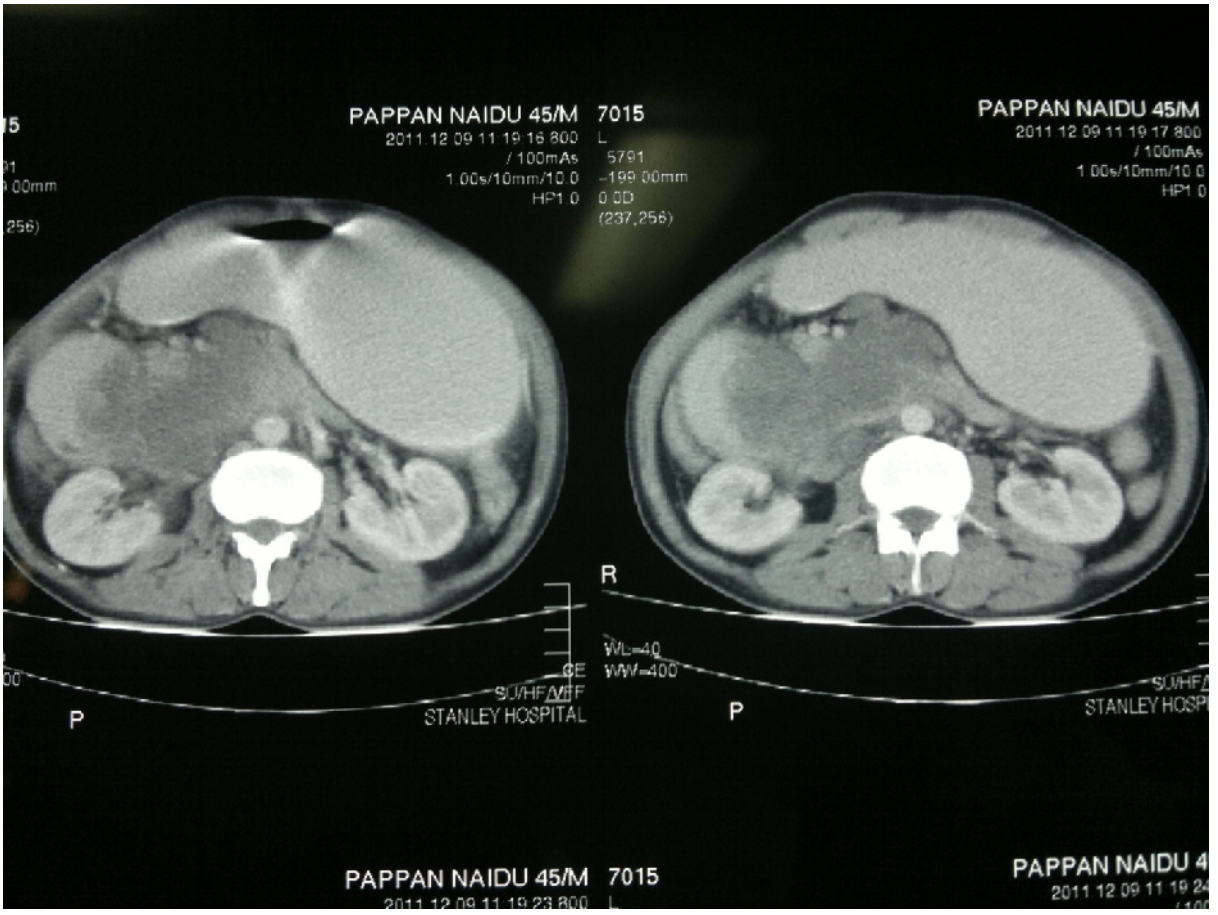


Fig 2-This CT scan shows a mass lesion in the head of pancreas,local infiltration into first and second portions of duodenum,and encasement of superior mesenteric pedicles.The disease was deemed inoperable pre operatively based on CT.His CA 19-9 levels was 18 U/L.Only a palliative bypass procedure was done.

ENDOSCOPIC ULTRASONOGRAPHY:(EUS)

EUS can image the primary cancer and be a means of obtaining a FNA of pancreatic adenocarcinoma, but in general the procedure is noncontributory when CT scan characterizes the tumor. When a mass cannot be visualized on CT scan, sonography through the wall of the stomach or duodenum can image tumors in the body/tail and head of the pancreas, respectively. EUS is also used to get tissue samples by EUS guided FNA. Although extremely sensitive in assessing the site,size, extent and vascular invasion, EUS cannot be used to detect nodal status or metastases and must hence be combined with CT or MRI scans.

MAGNETIC RESONANT CHOLANGIOPANCREATOGRAPHY(MRCP):

Owing to motion artifacts, lack of bowel opacification, low spatial resolution,long scanning times and low signal-to noise ratio, MRI has not been shown to have a definitive advantage over modern CT scanning[1] . Dynamic magnetic resonance imaging with rapid scanning sequences and bolus iv contrast administration, may have sensitivity and specificity comparable to those for helical CT[4] . The use of a cholangiopancreatography might further increase the sensitivity but there is no routine use of this imaging modality.

ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY(ERCP):

ERCP once was a very sensitive diagnostic test for pancreatic cancer[10]. The finding of an irregular stricture of varying lengths in the pancreatic duct also known as "double-duct sign" is a telltale sign of pancreatic malignancy . However, ERCP is no longer a diagnostic investigation. ERCP is seldom used if operative intervention is contemplated. Specific indications will include medically unfit or patients with inoperable,terminal disease just for biliary decompression.

ERCP delineates pancreatic duct and common bile duct anatomy.Brushings and ductal lavage are obtained and henceis a means of obtaining cytologic diagnosis. But, similar to EUS, in the face of a defining CT scan, its findings are often redundant. Pancreatitis, bleeding, and perforation are severe complications associated with ERCP and preclude the routine use of this modality in all

pancreatic cancer patients. ERCP should be reserved for patients in need of endoscopic stenting, equivocal findings on standard evaluation, or for patients in whom tissue diagnosis is needed, such as those in a clinical study, with advanced disease, or those anticipating neoadjuvant therapy. If anterior chemotherapy is being planned, an upper GI endoscopy would be

the first investigation. During this procedure, biliary outflow can be restored with the placement of an endobiliary stent, and EUS guided FNA can also be performed.[4]

PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAPHY(PTC):

This is another invasive technique of defining the biliary tree and better defines the proximal biliary anatomy above the level of obstruction. During this procedure a percutaneous biliary drain (PBD) can also be left in place for the relief of cholangitis. The disadvantages of PTC are a result of the more invasive nature of this technique and include bleeding, hemobilia, and patient discomfort, as well as the inability to visualize the pancreatic duct. For periampullary cancer, ERCP is more commonly used than PTC or PBD.

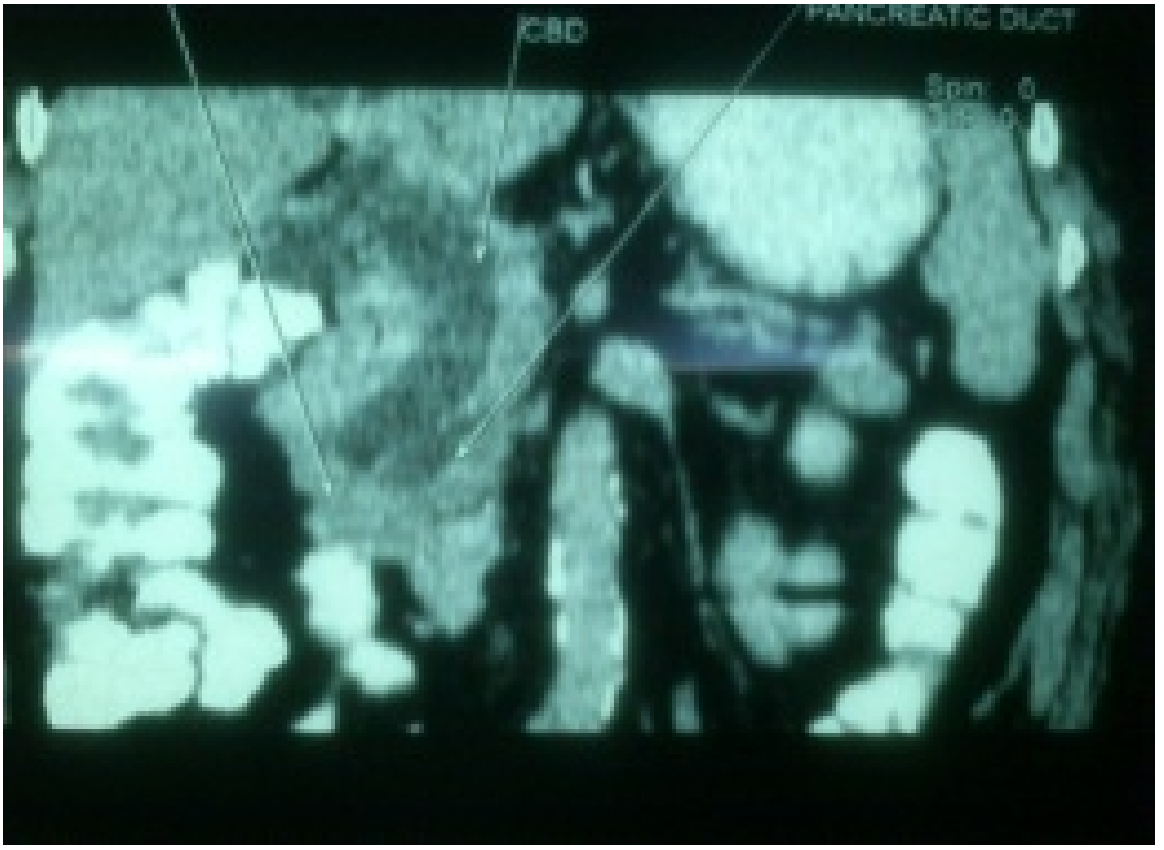


Fig 3-This MRCP image shows a mass lesion in the head of pancreas with dilated Common Bile Duct in the sagittal section.MRCP did not show signs of locally advanced or metastatic disease.But his CA 19-9 level was 50,000 U/l.Nevertheless, intraoperatively the tumor was completely resectable and a classical Whipple's procedure.

POSITRON EMISSION TOMOGRAPHY:(PET SCAN)

At present the role of PET scanning is not well defined for pancreatic cancers. However, more recent reports support the conclusion that FDG-PET imaging may have a supplementary role but PET scanning is not currently used in patients suspected of pancreatic cancers as a routine.

UPPER GI ENDOSCOPY:

Upper GI endoscopy is useful in the diagnosis of pancreatic cancers when these lesions infiltrate the ampullary region. If visualized, it is relatively straight-forward to obtain a biopsy . Additionally, endoultrasound may be performed during this procedure to visualise the ampulla and duodenum [18]. Fine-needle aspiration (FNA) of any suspected lesions can be performed at the same time as endoscopic ultrasound if tissue diagnosis is of benefit.

Fig-4 This is a picture of an Upper GI endoscopy which shows a growth in the region of the ampulla.The CT scan showed a mass lesion in the head of pancreas which was locally advanced and had infiltrated along the papilla to reach the periampullary region.

STAGING LAPAROSCOPY:

Currently, routine use of laparoscopy is not warranted. Few patients will have findings on laparoscopy that add to information found at CT scanning. It is recommended that Laparoscopy be limited to select patients with primary tumors greater than 2 cm in diameter, body or tail tumors, equivocal findings of metastasis on CT, ascites, and subtle clinical or laboratory findings such as hypoalbunemia, elevated CA 19-9, marked weight loss, and pain with narcotic dependency. Using these criteria, the subset of patients with advanced tumors not identified on CT scan can be accurately assessed by laparoscopy, and patients likely to not have additional findings can be spared the expensive, time-consuming procedure.

TISSUE DIAGNOSIS:

In a patient with a pancreatic mass who appears resectable and is a good operative candidate this still remains somewhat controversial. Percutaneous pancreatic mass biopsies can easily be performed, but malignancy cannot be ruled out in case of a negative smear[35]. They can be performed safely with rare complications including, fistula, pancreatitis, hemorrhage, abscess, tumor seeding and rarely death[10]. A negative biopsy in a patient suspected of having pancreas cancer with a low operative risk

and apparently resectable disease will not alter the decision to explore the patient. Percutaneous biopsies should only be performed in patients thought to have prohibitively high operative risks or who appear unresectable and are being considered for either neoadjuvant or palliative therapy. In special circumstances as a result of a patient presenting imaging characteristics where lymphoma or metastatic disease from another primary are suspected, percutaneous biopsy has value. These diseases are often best managed without resection. FNA may be performed at the same time as endoscopic ultrasound (EUS).

TUMOR MARKERS:

Tumor markers are indicators of cellular, biochemical, molecular, or genetic alterations by which neoplasia can be recognized. These surrogate measures of the biology of the cancer provide insight into the clinical behavior of the tumor. This is particularly useful when the cancer is not clinically detectable. The information provided may

- Be diagnostic and distinguish benign from malignant disease
- Correlate with the amount of tumor present (so-called tumor burden)
- Allow subtype classification to more accurately stage patients

- **B**e prognostic, either by the presence or absence of the marker or by its concentration
- Guide choice of therapy and predict response to therapy

The features of an ideal tumor marker: [32]

1. The marker is expressed exclusively by the particular tumor
2. Collection of the specimen for the tumor marker assay is easy.
3. The assay itself is reproducible, rapid, and inexpensive.
4. Currently, there is no one marker that fulfills all these criteria for any cancer, nor is there any specific cancer in which there are biomarkers that completely describe its behavior.
5. Tumor markers fall into three broad categories—proteins, genetic mutations, and epigenetic changes. All three may be found in the tumor tissue itself. Tumor markers found in body fluids, particularly blood and urine, have the greatest potential for clinical application because of the ease of access to these fluids for analysis and because repeated sampling allows in vivo monitoring of the malignancy for such features as disease progression or recurrence, metastasis, and response to therapy.

CLASSIFICATION OF TUMOR MARKERS:

RNA- Based Markers

Overexpressed/underexpressed transcripts

Regulatory RNA (e.g., micro-RNA)

DNA-Based Markers

Single-nucleotide polymorphisms (SNPs)

Chromosomal translocations—*bcr-abl* (Philadelphia)

Changes in DNA copy number

Microsatellite instability

Epigenetic changes (e.g., differential promoter region methylation)

Carbohydrate Antigen 19-9

Carbohydrate antigen 19-9 (CA 19-9) is widely used as a serum marker for pancreas cancer, but its use is limited to monitoring response to therapy, not as a diagnostic marker. It is a mucin-type glycoprotein expressed on the surface of pancreatic cancer cells and was initially detected by monoclonal antibodies raised against colon cancer cell lines in a mouse model.[7] The CA 19-9 epitope is normally present within the biliary tree. Biliary tract disease, both acute and chronic, can elevate serum CA 19-9 levels.

TESTING:

CA 19-9 is detected with an immunoassay, and the upper limit of normal for a healthy adult is 37 U/mL. Sensitivities of CA 19-9 in the diagnosis of pancreatic cancer range from 67% to 92%, with specificities ranging from 68% to 92%.[7] The utility of CA 19-9 as a diagnostic marker is limited in a number of ways. First, patients withLewis blood group negative antigen cannot synthesize CA 19-9, and therefore is not used as a marker in them, who make up about 10% of the population. Second, patients with benign biliary tract disease can have levels up to 400 U/mL, with 87% having concentrations higher than 70 U/mL. Significant numbers of patients with pancreatitis, either acute or chronic, also have elevated levels. Third, CA 19-9 levels are also elevated in those with other cancers, including those of the biliary tree (95%), stomach (5%), colon (15%), liver (HCC, 7%) and lung (13%). For colorectal cancer, CA 19-9 levels add little clinically useful information to determination of CEA levels.

SCREENING:

It is not useful as a screening modality because of its low sensitivity in early-stage disease. With increasing levels, the diagnosis of pancreatic malignancy becomes more accurate. When a cutoff level of 100 U/mL is

used, a number of studies have demonstrated that although sensitivity ranges from 60% to 84%, specificity for pancreas cancer is 95% or greater. Levels higher than 1000 U/mL are almost diagnostic of pancreatic cancer. Because of its frequent elevation in benign biliary tract disease,it is not useful in distinguishing benign from malignant distal common bile duct strictures.

PROGNOSIS:

In patients with pancreatic cancer , the level of CA 19-9 has been shown to correlate with tumor burden.[21] For example, higher levels typically correlate with higher tumor stage, and more than 95% of patients with unresectable disease have levels higher than 1000 U/mL. Of patients who undergo curative resection, those whose CA 19-9 levels returned to normal survived longer than those whose levels fell but never normalized.

MONITORING:

Serial measurement of CA 19-9 is used to monitor response to treatment. A rise in CA 19-9 after curative resection has been shown to precede clinical or computed tomographic evidence of recurrence by 2 to 9 months. In patients with unresectable/metastatic disease, failure of CA 19-9 levels to fall with chemotherapy reflects poor tumor response. However, in both

settings, the lack of alternative effective therapies limits the utility of serial monitoring of CA 19-9.

TREATMENT METHODS:

WHIPPLES PANCREATICODUDENECTOMY:

Exposure for a pancreaticoduodenectomy can be performed through a midline laparotomy incision or a chevron incision can be used.

The first step of the pancreaticoduodenectomy is to assess the extent of disease and resectability.After entering the abdomen thorough search for deposits in the liver surface,pelvis,mesentry and parietal peritoneum is done. An extended Kocherisation is performed by creating a plane between the retroperitoneum and duodenum+ head of the pancreas allowing the visualization of the superior mesenteric artery at its origin .The lesser sac is entered by dividing the gastrocolic omentum from the colonic end and the tumor is held between the thumb and index finger and the local extension is assessed.[26]

When the tumor is deemed resectable gall bladder is mobilised from the fossa and a cholecystectomy is done.The common hepatic duct is divided distal to the insertion of the cystic duct. The portal vein tunnelling is done in the TUNNEL OF LOVE[6] ,in the retropancreatic groove.The

portal vein is skeletonised from the neck of pancreas upto the porta hepatis.[8]The gastroduodenal artery is identified, clamped and ligated.

For a classic Whipple procedure, a distal gastrectomy is performed by dividing at the level of D 1. In a pylorus-preserving pancreaticoduodenectomy, the stomach is divided 2 to 3 cm distal to the prepyloric vein of Mayo with a linear stapling device.[12] Distally the bowel is divided 20 cm distal to the ligament of Treitz..[1]

The SMV PV confluence is identified and an avascular plane is developed nterior to it after ligating the multiple small tributaries draining into the SMV.Inadvertant injury to these vessels might cause torrential intraoperative bleeding.Once the plane is created a penrose drain is passé across at the level of neck of pancreas. Two stay sutures are taken ,one superiorly and the other iinferiorly before the pancreas is transacted at the neck and the duct orifice in the pancreatic remnant is cannulated. More stay sutures with 2 ‘0 silk are used in the remnant and a plan is being made for reconstruction

There are multiple options for reconstruction after pancreaticoduodenectomy. Most commonly the reconstruction first involves the pancreas, then the biliary, and lastly the enteric.

The first anastomosis is pancreatic either a pancreaticogastrostomy or pancreaticojejunostomy.The pancreaticojejunostomy is done in an end to end or end to side fashion using 2 ‘0 vicryl and 2 ‘0 silk in two layers.[12] The pancreaticogastrostomy is usually done by the dunking method in two layers.The next anastomosis is the hepaticojejunostomy done in a single layer by the parachuting technique with 3’0 silk.The anastomosis is positioned 10 to 15 cm distal to the pancreatic anastomosis. The continuity of the bowel is established by a gastrojejunostomy 20 to 30 cm distal to the bilioenteric anastomosis.The gastrojejunostomy is done in a retrocolic,isoperistaltic fashion in 2 layers with 2 ‘0 silk and 2’0 vicryl.A feeding tube is placed distal to all the anastomoses.Bilateral intraperitoneal drains are placed and wound closed in layers.

The postoperative management consists of keeping the patient with nothing by mouth for atleast 4 to 5 days. The stomach is decompressed with a nasogastric tube which is positioned intraoperatively to drain the bile.It is removed when the outpu falls below 500 ml. Feeding through the jejunostomy tube is initiated by third post operative day as tolerated and gradually stepped up till 2.5 litres. In case of suspicion of a leak DT amylase is measured in relation to the serum amylase.The drains around the pancreatic anastomosis are removed when there is no evidence of leak.

Multiple theoretic justifications to place preoperative biliary stents exist, including better delineation of the level of obstruction, reduction of jaundice and pruritus, increased ease in performing the bilio enteric anastomosis, prevention of biliary sepsis.[12] Currently stenting is done only when indicated.

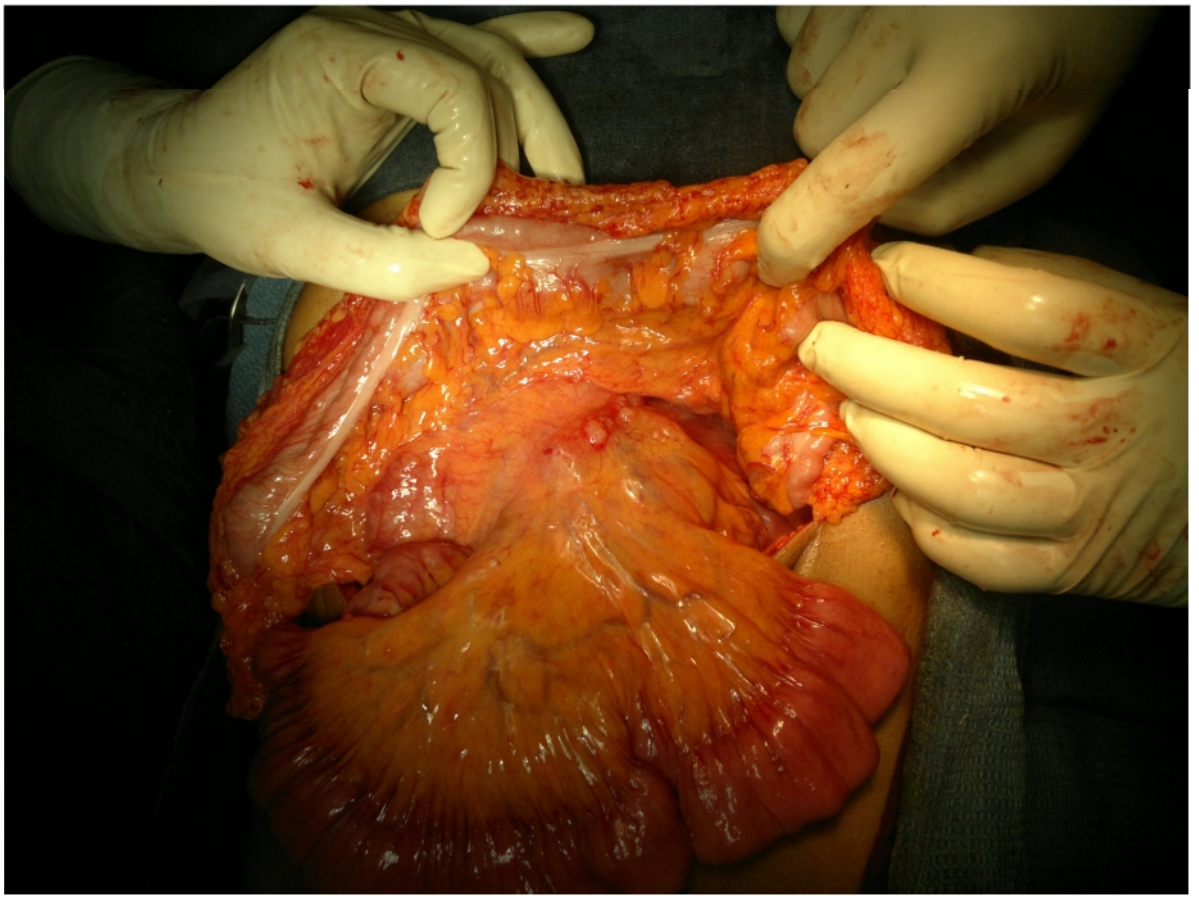


Fig 5-During initial assessment, during laparotomy ,multiple deposits

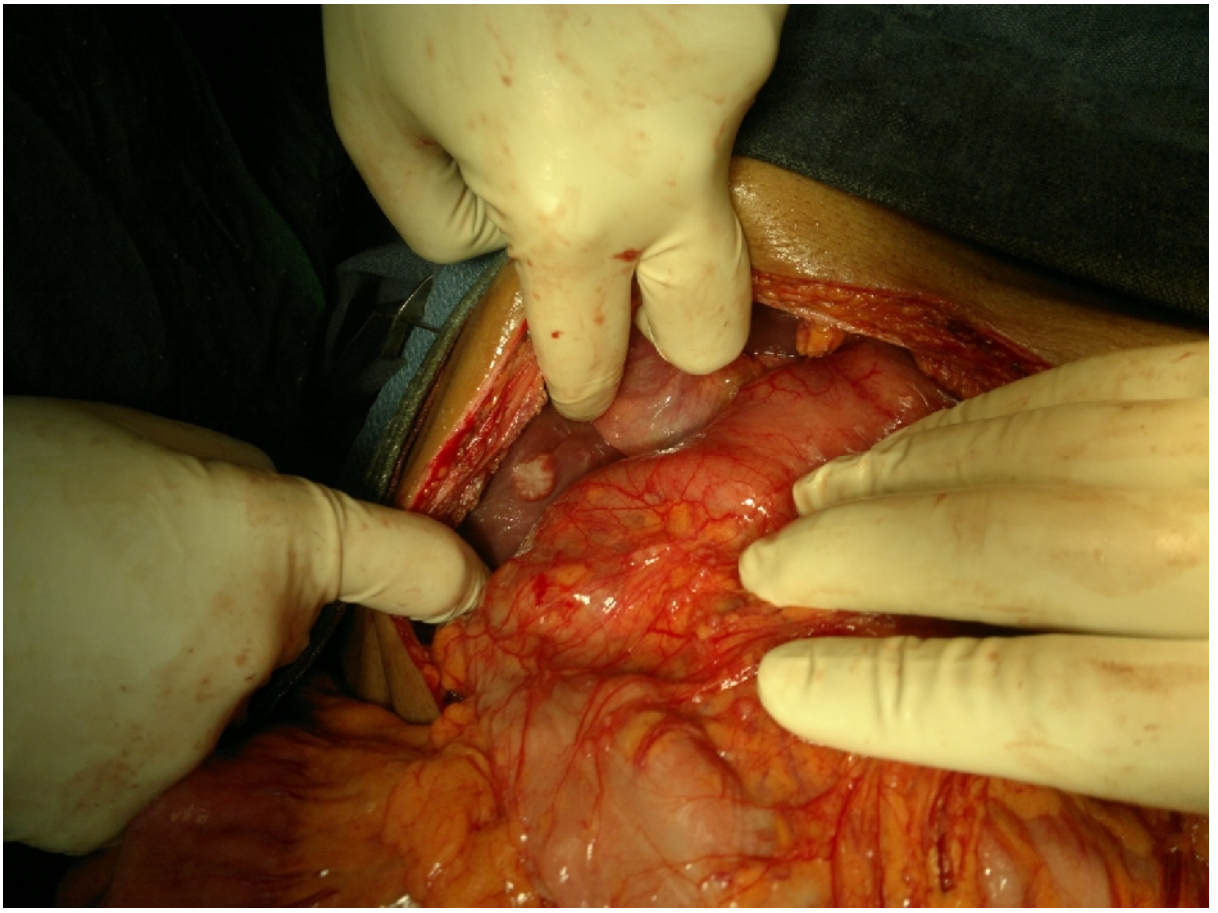


Fig6- Surface deposits found in the liver,the disease was metastatic and was inoperable.Only a palliative bypass was done. were found in the mesentry and transverse mesocolon.The disease was metastatic and only palliative bypass was done.

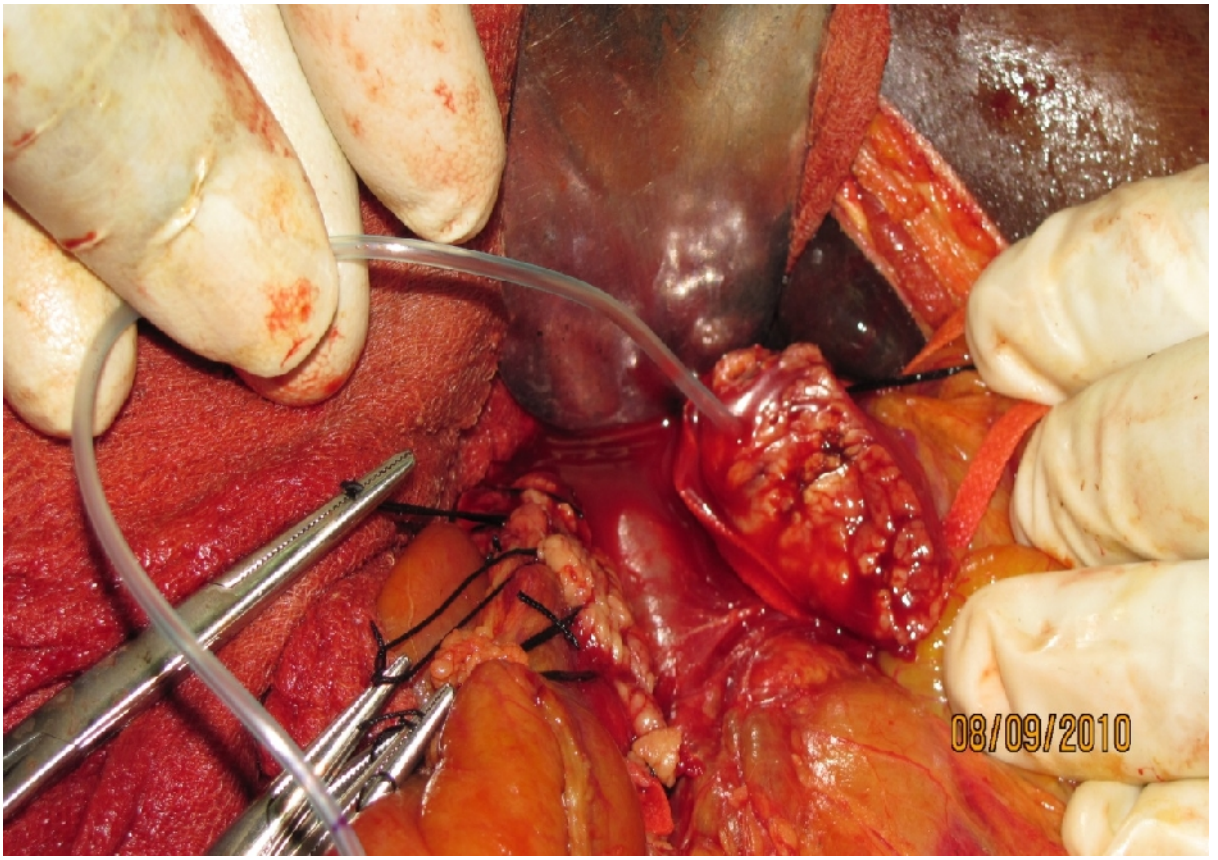


Fig 7-Pancreas transacted at the neck after taking stay sutures superiorly and inferiorly.The pancreatic duct is cannulated to allw pancreatico jejuna anastomosis-duct to mucosa anastamosis.

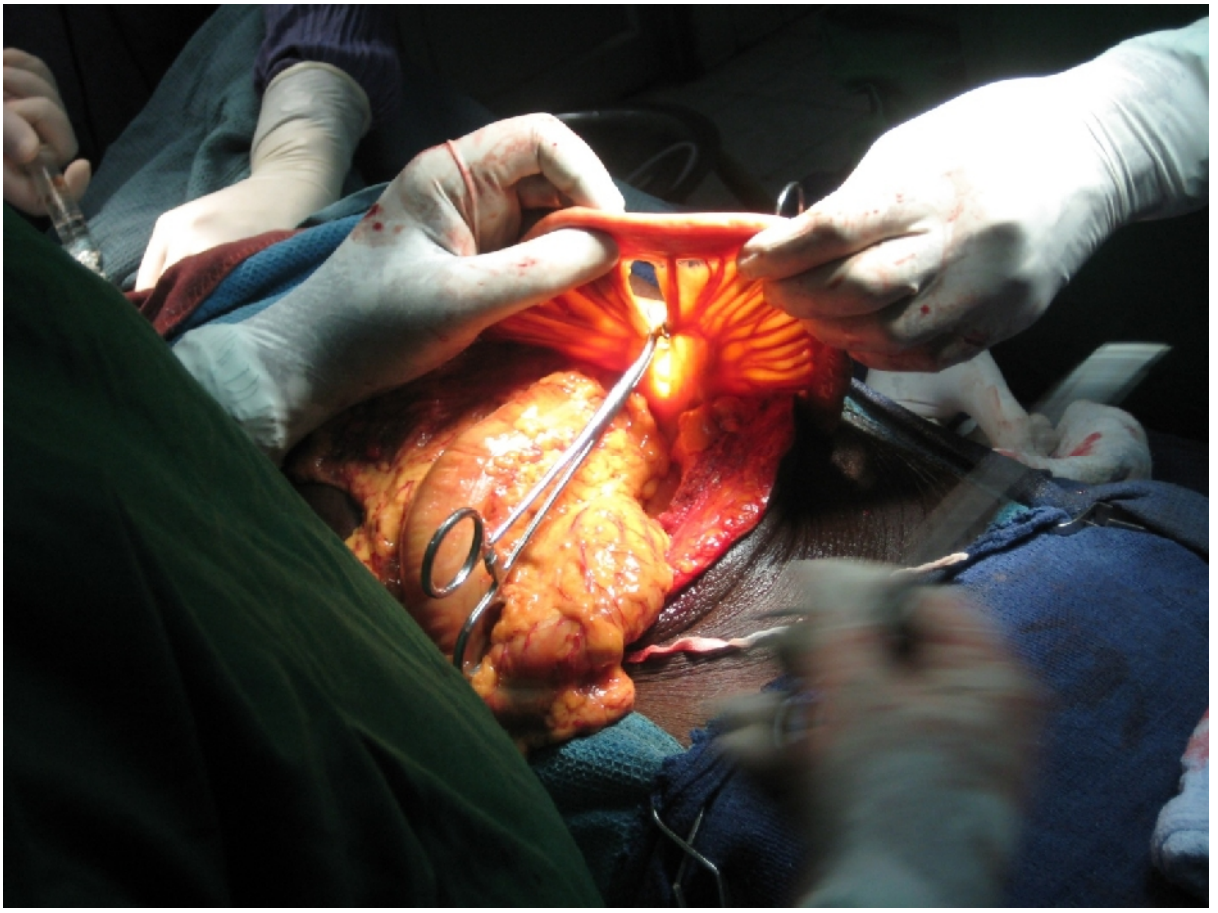


Fig 8- Roux loop is being constructed by dividing the vessels in the mesentry and 20 cm from the DJ flexure is removed with the specimen.

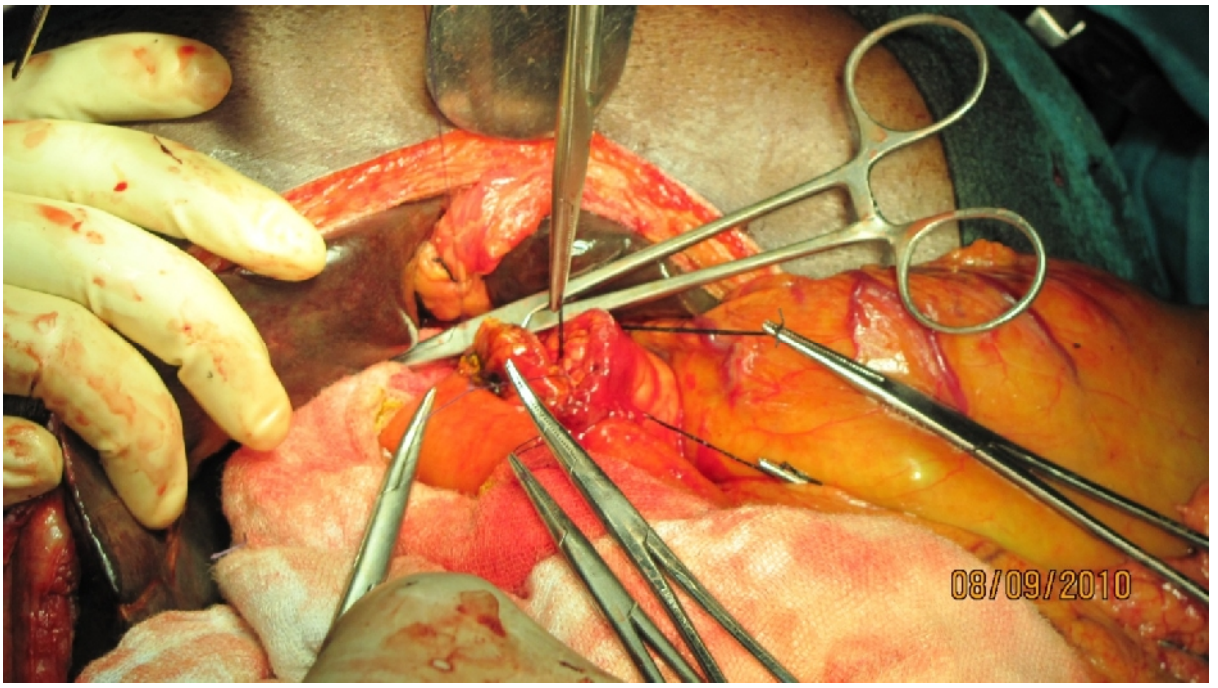


Fig 9- Pancreatico jejunostomy ,the first anastomosis of whipples procedure is being done in an end to end fashion in 2 layers.

Fig 10- Roux en Y hepatico jejunostomy done 15 cm distal to pancreatico jejunostomy,done in single layer with 3’0 silk.

Fig 11-Cut section of the specimen including distal stomach,gall bladder with cystic duct,entire duodenum and first 20 cm of jejunum.The instrument is pointing at the ampulla with a stent in situ,which was placed preoperatively for biliary decompression.

COMPLICATIONS:

The operative mortality rate for Whipples procedure is currently less than 2% in centers specializing in pancreatic surgery.[2] Despite this, the incidence of postoperative morbidity remains as high as 40 to 50%. The two leading causes of postoperative morbidity are early delayed gastric emptying and minimal leak or dehiscence at the pancreatic anastomosis (pancreatic fistula). Delayed gastric emptying is seen in up to15% of patients. Although not endangering and usually self-limiting, this condition can prolong lengths of stay and increase hospital cexpenditure.. Erythromycin, a motilin agonist, may improve gastric emptying after pancreaticoduodenectomy. Pancreatic fistula occurs in 10 to 20% of patients after pancreaticoduodenectomy. [10]The pancreatic anastomotic leak is usually managed by placing closed-suction drains close to the pancreatic anastomosis, to make it a controlled fistula and to reduce the risk of intra- peritoneal abscess. By definition, a pancreatic fistula usually occurs 7 or more days postoperatively, when the output in the drainage tubes contain milky, amylase-rich fluid of atleast 50 ml per day.[1]When the amylase level in the drainage tube fluid is three times raised over the serum amylase it is pathognomonic of pancreatic anastomotic leak. In approximately 85% of patients, the pancreatic leak settles withconservative

management, 10% will require image guided aspiration of the loculated collection,5% may require exploration for adequate peritoneal lavage. Other significant complications[1] :

Wound infection

Intra-abdominal abscess

Cholangitis

Pneumonia

Bile leak

Pancreatitis

PALLIATIVE THERAPY:

With accurate preoperative staging, the resectability rate for periampullary cancers is approximately 80%. When a patient undergoes exploratory laparotomy (and sometimes exploratory laparoscopy) and is found to be unresectable, a decision must be made as to whether to operatively palliate the patient. Operative palliation is indicated in a patient without widespread metastatic disease and with a relatively long life expectancy. The added potential morbidity and mortality of operative palliation must be weighed against the more durable palliation achieved with hepaticojejunostomy and/or gastrojejunostomy. Additionally,

chemical splanchnicectomy can be performed at the same time for relief of pain.

Operative Palliation of Obstructive Jaundice:

The most commonly performed procedure for biliary decompression is hepaticojejunostomy. Simple drainage through a T tube inserted above the biliary obstruction should be avoided as this causes a high output biliary fistula and results in major electrolyte abnormalities. Hepaticojejunostomy provides more durable relief of obstructive jaundice than does cholecystojejunostomy because of the proximity of the cystic duct to most periampullary cancers. The hepaticojejunostomy is performed after cholecystectomy in an end-to-side fashion to either a Roux limb or a loop of jejunum with a Braun jejunojejunostomy between the afferent and efferent limbs. Only 4% of patients with unresectable periampullary cancers palliated with hepaticojejunostomies develop recurrent jaundice prior to their deaths. As operative palliation is attempted more with minimally invasive techniques, perhaps laparoscopic cholecystojejunostomies will be performed more often secondary to the relative ease with which they can be done and to avoid a major incision.

Operative Palliation of Duodenal Obstruction:

Pancreatic cancers may cause gastric outlet obstruction by compromising the duodenal lumen. Most patients with gastric outlet obstruction from a pancreatic cancer that is not widely disseminated benefit from palliation, whether operative or with endoscopic stenting techniques. There remains controversy, however regarding the role of prophylactic gastrojejunostomy in a patient who is being explored but without symptoms of gastric outlet obstruction. The gastrojejunostomies were performed typically in a retrocolic (to the left of the middle colic vessels) and isoperistaltic fashion, using a loop of jejunum 20 to 30 cm beyond the ligament of Treitz.[6] The gastrotomy is placed on the back wall of the stomach in the most dependent portion. Vagotomy is not routinely done because it might worsen the delayed gastric emptying, the limited life expectancy of the patients, and the ability to control acid secretion medically.

Operative Chemical Splanchnicectomy for Pain:

The procedure is performed by injecting 20 mL of 50% ethanol or saline through a spinal needle in the para aortic space at the level of the celiac plexus. Even those patients who did not report pain preoperatively derived benefit from the splanchnicectomy as they appeared to have a

delay in the onset of their pain and had lower pain scores as their disease progressed when compared to control patients.

Nonoperative Palliation:

Only 15–20% of patients with pancreas cancer are found to be resectable[5] for cure at the time of presentation because of disseminated disease or locally advanced diseaseFor the majority of patients, palliation of symptoms is the primary goal of any invasive intervention,and the three main problems that need to be palliated are obstructive jaundice, gastric outlet obstruction, and pain.

Nonoperative Palliation of Obstructive Jaundice:

Nonoperative biliary drainage can be achieved either through a percutaneous or an endoscopic approach. Percutaneous transhepatic approaches are aided by the fact that the intrahepatic ducts are usually dilated in patients presenting with obstructive jaundice. Endoscopic drainage has the advantage of not having any external catheters. In a randomized trial comparing endoscopic versus percutaneous stent placement in 70 patients, the success rate, overall complication rate, and procedure related mortality rate was significantly lower in the endoscopic group. Endoscopic biliary stents may be either plastic or metal. Plastic

stents are generally temporary and are available in different diameters and lengths. Because of the limitations in the diameter of the accessory channel of endoscopes, usually the largest plastic stent that can be placed is 12F. This relatively small diameter results in frequent occlusion and the necessity of periodically changing these stents. In an effort to improve on the rate of stent occlusion, self-expanding metallic stents have been developed and when deployed can reach a diameter of 30F. Randomized controlled clinical trials comparing 10F or 11.5F plastic stents to 30F metallic stents have shown metallic stents to have a longer patency rate (6.2 to 9.1 months compared to 4.2 to 4.6 months) and to be associated with lower rates of cholangitis, stent replacement/revision, and hospital days. Metallic stents eventually fail because of tumor ingrowth at the ends and through the interstices. Polyurethane-covered stents are currently being developed and used and probably have better patency and results. The disadvantage of metallic stents is that they cost more and should be used in patients who are expected to live longer than 6 months.

Nonoperative Palliation of Duodenal Obstruction:

Until recently, duodenal obstruction in patients found to be unfit for surgical bypass was treated with placement of gastrostomy tubes. The development of expandable metallic bowel stents have provided an

additional way of controlling gastric outlet obstruction in this group of patients. Gastroduodenal stenting is successful in 80–90% of patients and provides adequate relief of obstruction in most patients.

Nonoperative Palliation of Pain:

In addition to opioids and nonsteroidal anti-inflammatory agents, several nonoperative palliative treatment modalities for pain with periampullary cancers have been developed including ultrasound or CT-guided celiac plexus nerve blocks and even external beam radiotherapy. Several randomized controlled clinical trials comparing percutaneous celiac plexus nerve blocks to standard oral analgesics have demonstrated significant diminution in pain and narcotic use in the majority of the patients.

ADJUVANT THERAPY:

In 1985, the Gastrointestinal Tumor Study Group (GITSG) trial was published. This was a prospective randomized trial to split-course radiotherapy (4000 cGy, 20 fractions, over 6 weeks) with bolus 5-flourouracil (5-FU) 500 mg/m^2 [16]intravenous daily, each of the first three days of radiation therapy of each 200-cGy sequence in patients with pancreas cancer. Additionally, patient receiving adjuvant therapy received

bolus 5-FU every week for 2 years. The patients on this trial who received adjuvant therapy had better overall survival rates.

It has also been demonstrated that multiagent 5-FU based chemotherapy regimens can be combined with radiotherapy. The various drugs which can be used are cisplatin,interferon gama,gemcitabimne

NEOADJUVANT THERAPY:

Neoadjuvant therapy has several theoretical advantages. It allows timely administration of chemo- or chemoradiotherapy to patients who are at a high risk of residual or recurrent disease following surgical resection. It has the potential to shrink the tumor and can decrease the extent of local disease. Patients who develop dissemination during neoadjuvant treatment are unlikely to gain advantage from surgical resection and are spared the morbidity, and potential mortality of resection. It allows better patient selection who are most likely to benefit from surgical resection

PALLIATIVE CHEMOTHERAPY:

Prior to the (FDA) approval of gemcitabine, the antimetabolite 5-FU was considered standard therapy for advanced pancreatic cancer. Although response rates greater than 30% were reported for treatment with 5-FU[17], most of these reports were based primarily on clinical tumor

evaluation. But currently more modern phase II trials have reported response rates less than 10% for 5-FU alone or with leucovorin.[11]

Gemcitabine is a nucleoside analogue that is sequentially phosphorylated and incorporated into replicating DNA,and that would cause premature chain termination.[11] Through use of this agent, significant tumor shrinkage by more than 50% was achieved in only about 5% of patients, but a substantial subset of patients had sustained alleviation of tumor-related symptoms.Trials are currently being conducted by combining gemcitabine with other chemotherapeutic agents such as topoisomerase I inhibitors, platins, and taxanes. Additionally, gemcitabine is being combined with targeted therapy agents such as antiangiogenic and epidermal growth factor receptor agents

IMMUNOTHERAPY:

Immune-based therapies can exploit both the cellular and humoral components of the immune system. Strategies directed at the cellular components recruit and activate T cells that recognize tumor-specific antigens.[14] Strategies using monoclonal antibodies are being designed to target tumor-specific antigens that can kill tumor cells by direct lysis or

through delivery of a conjugated cytotoxic agent. Both approaches are attractive for several reasons.

PROGNOSTIC FACTORS OF CARCINOMA OF PANCREAS:

The prognosis for patients with resected adenocarcinoma of the head of the pancreas is predicted by multiple factors including[12]

- ✓ tumor stage
- ✓ biologic features
- ✓ molecular genetics
- ✓ degree of differentiation
- ✓ margin status
- ✓ nodal status
- ✓ perioperative factors
- ✓ the use of adjuvant chemoradiation.

In an analysis of long-term survivors with resected pancreatic adenocarcinoma, the 5-year actual survival rates was 15% for pancreatic cancers.

CONCLUSION:

Pancreatic cancers represent significant clinical problems. Although traditionally patients with these diseases had a dismal prognosis, proper staging and patient selection have led to improved results. When possible, surgical resection for cure should be attempted as this gives the only chance of long-term survival. Surgical resection should be performed by surgeons experienced in the management of these diseases and at centers that can aptly care for these patients to minimize morbidity and mortality. There are many developments on the horizon that have the potential to improve the survival and well-being of patients with these diseases.

To summarise,tumor markers are generally helpful as part of a diagnostic work-up, in prognosis, and as surrogates of tumor burden. In pancreatic cancer, several tumors markers may be elevated including CEA, the carbohydrate antigens (CA) 19-9, 50, and 242, CAM 17-1, and DUPAN 2. Of these, CA 19-9 has emerged as the most clinically useful marker. This antigen was originally defined by a monoclonal antibody produced by hybridomas from mice inoculated with a human colon cancer cell line. The epitope of this antibody is a sialylated lacto-N-fucopentaose II related to the Lewis-a blood group antigen. This underscores the limitations of CA 19-9. First, it is not specific for pancreatic cancer and

has been found to be elevated in a number of other tumor types such as biliary tract, colon, and stomach cancers. Second, roughly 10% of patients are Lewis antigen-a or -b negative and unable to synthesize this antigen. These individuals have undetectable levels of CA 19-9, even in the setting of advanced pancreatic cancer.[35] Furthermore, cholestasis can falsely elevate serum CA 19-9 levels and, therefore, in patients who present with obstructive jaundice, an elevated CA 19-9 is not specific for the presence of pancreatic malignancy. Despite these caveats, serum CA 19-9 levels appear to have prognostic utility, particularly when measured either preoperatively and/or postoperatively in patients with resectable pancreatic cancer. In addition, for patients with more advanced disease, a decrease in CA 19-9 levels in response to therapy has been associated with better survival.Although serum CA 19-9 levels have clinical utility in established pancreatic cancer, its performance as a screening tool has been disappointing.

In the evaluation of patients, preoperative CA 19-9 levels have been used to predict patient outcomes. When blood levels of CA 19-9 were greater than 1000 U/mL, 96% of tumors were found to be unresectable. However, this preoperative evaluation alone has yet to be widely used to establish inoperability.[1] Furthermore, several studies have shown a correlation between a postoperative decline in CA 19-9 levels and the

increased duration of patient survival. Patients whose CA 19-9 normalized postoperatively may live longer , whereas rising CA 19-9 levels may correlate with shorter survival time.Currently since inconclusive data exixts regarding the value of CA 19 9 to predict the reseectability of tumor in the head of pancreas it is imperative to do an analysis of the same in our setting.

AIMS AND OBJECTIVES

AIMS AND OBJECTIVES:

The aim of the present study is

- To analyze the relation of the tumour marker CA 19-9 levels to the stage of the disease in cancer head of pancreas and
- To evaluate its role in predicting the tumour resectability.

MATERIALS AND METHODS

METHODS:

A proforma will be made that includes detailed history, physical examination, basic investigations and other relevant investigations required. All patients diagnosed with carcinoma head of pancreas on the basis of CECT Abdomen & Pelvis or MRCP,will be tested for serum levels of CA 19-9. On the basis o fthe mentioned inclusion and exclusion criteria 30 patients who are eligible are included in the study.After complete evaluation, these patients are taken up for surgery with either curative or palliative intent.The intraoperative findings, based on which the resectability of the tumour is ascertained are documented..Postoperatively,diagnosis is confirmed by the histopathological report of either the resected specimen(curative surgery) or tissue sampling (palliative surgery). Subsequently ,the correlation between the levels of CA 19-9 and the resectability of the tumour are analysed.

MATERIALS:

• Setting	:	Department of General Surgery, Government Stanley Hospital, Chennai
• Study design	:	RETROSPECTIVE ANALYTICAL STUDY
• Study period	:	2 years
• Materials	:	30 patients
• Inclusion criteria	:	Age 30-80 years Both male and female patients Patients with carcinoma head of pancreas proven by CECT/MRCP
• Exclusion criteria	:	Patients not taken up for surgery, either curative or palliative.
• Ethical committee clearance	:	Obtained
• Informed consent	:	Obtained

RESULTS AND ANALYSIS

Table 1:

SITE OF MALIGNANCY	MALE	FEMALE
HEAD OF PANCREAS	16	14

GENDER DISTRIBUTION

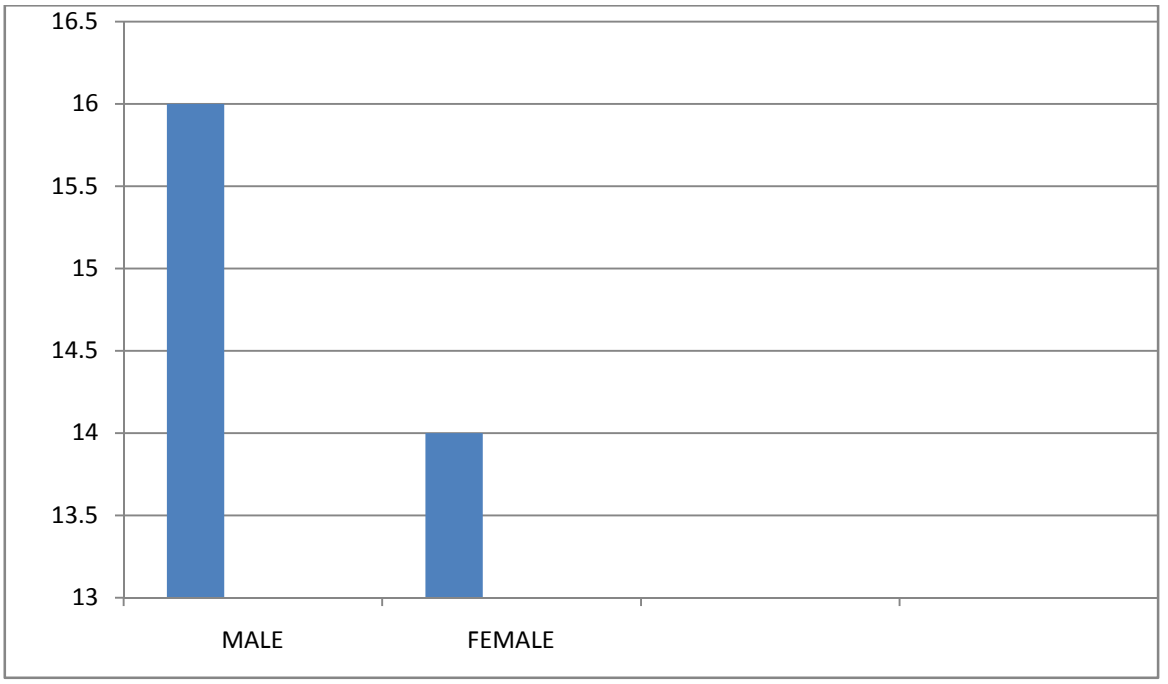


Table 2:

AGE GROUP	31-40	41-50	51-60	61-70	71-80
NO.OF PATIENTS	6	4	10	9	1

AGE DISTRIBUTION

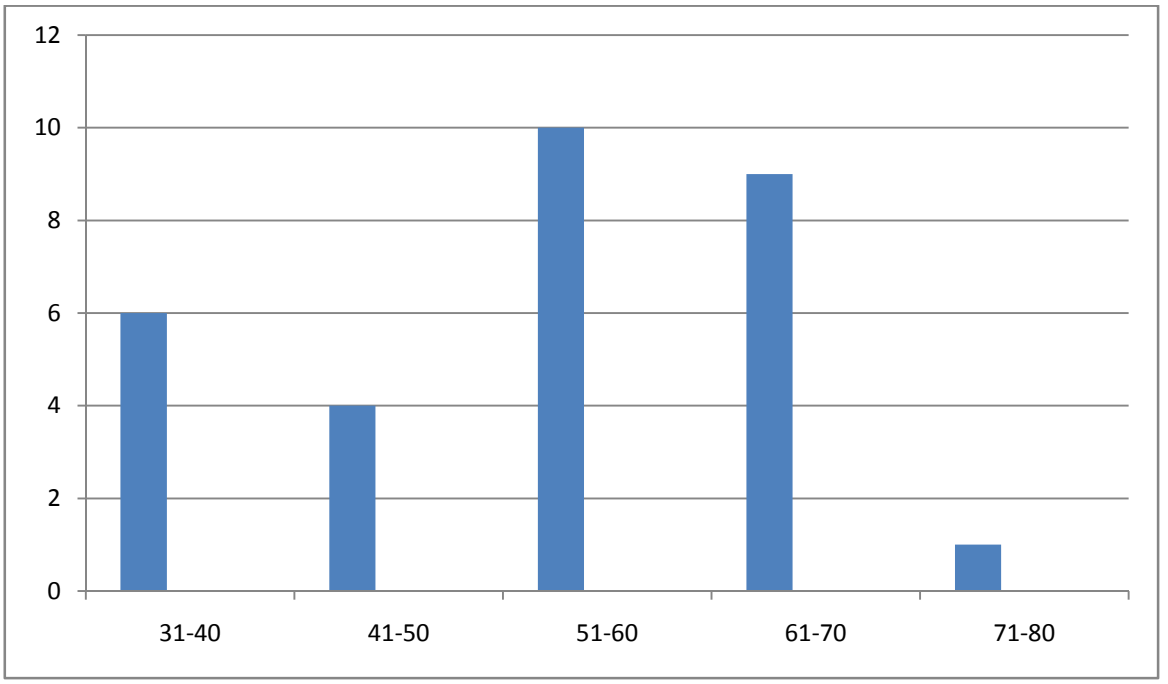


Table 3:

TUMOR MARKER	<37 U/L	>37 U/L
CA 19-9	21	9

DISTRIBUTION OF CA 19-9 LEVELS

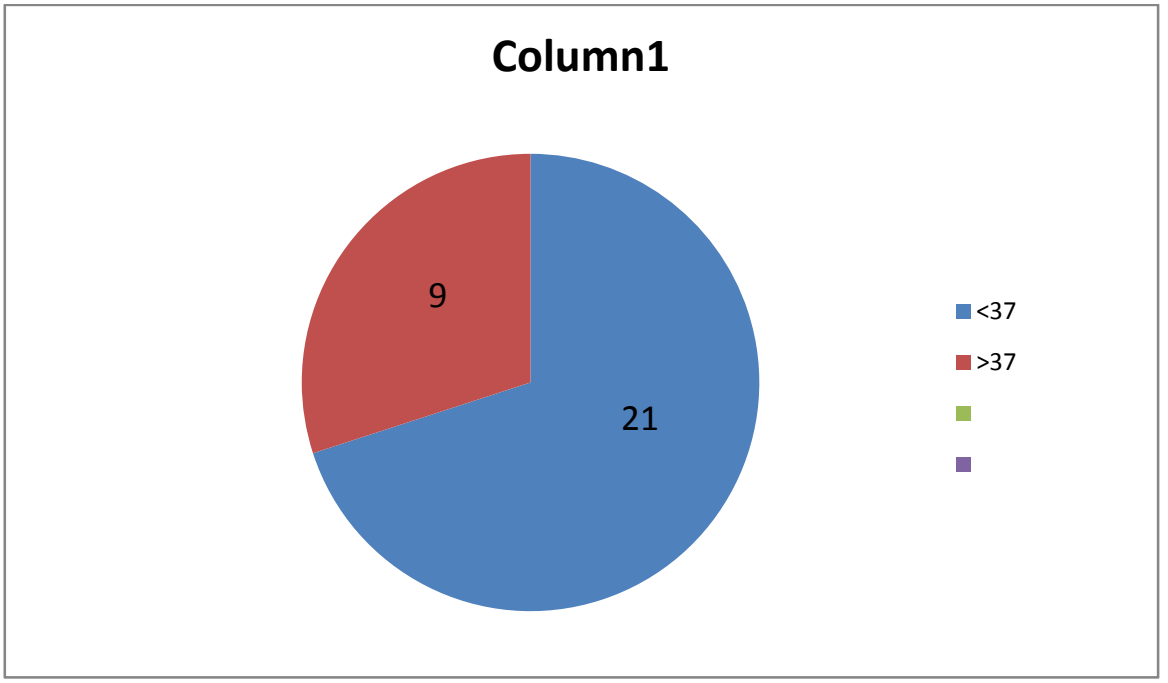


Table-4

NATURE OF SURGERY	WHIPPLES PROCEDURE	PALLIATIVE BYPASS
NO.OF CASES	13	17

NATURE OF OPERATIVE PROCEDURE:

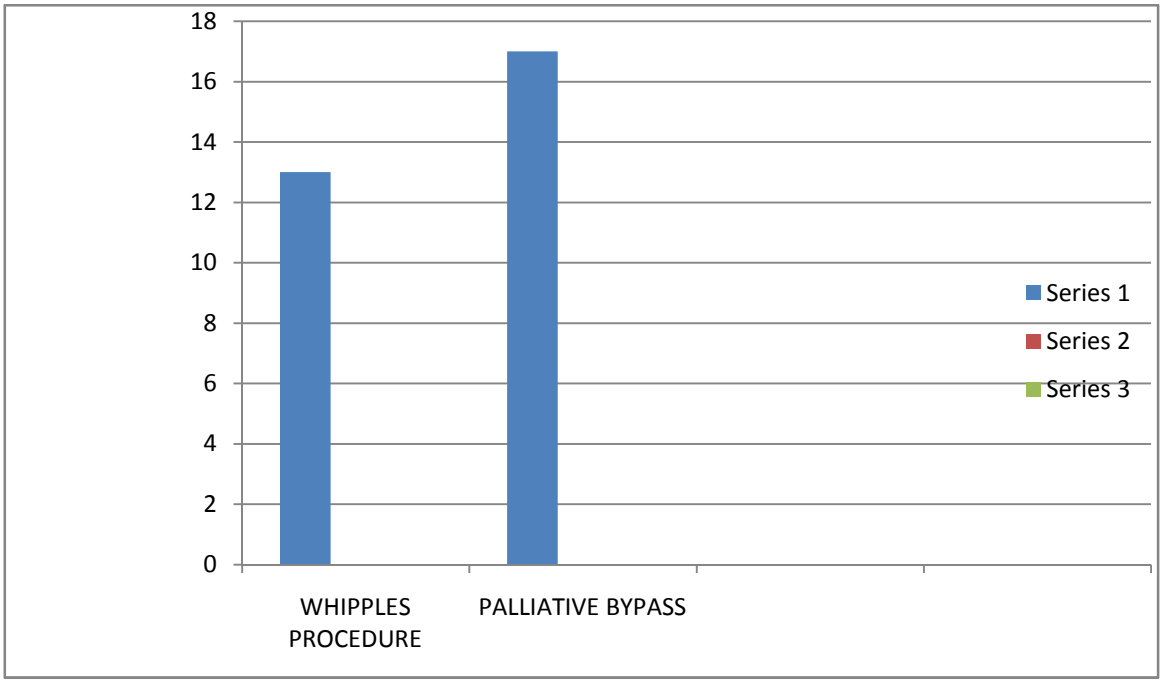


Table-5

LEVELS OF CA 19-9	PREOPERATIVELY INOPERABLE	INTRAOPERATIVELY INOPERABLE	TOTAL NUMBER OF CASES
<37	6	6	12
>37	2	3	5
NUMBER OF CASES	8	9	17

CA 19-9 LEVELS AMONG INOPERABLE CASES

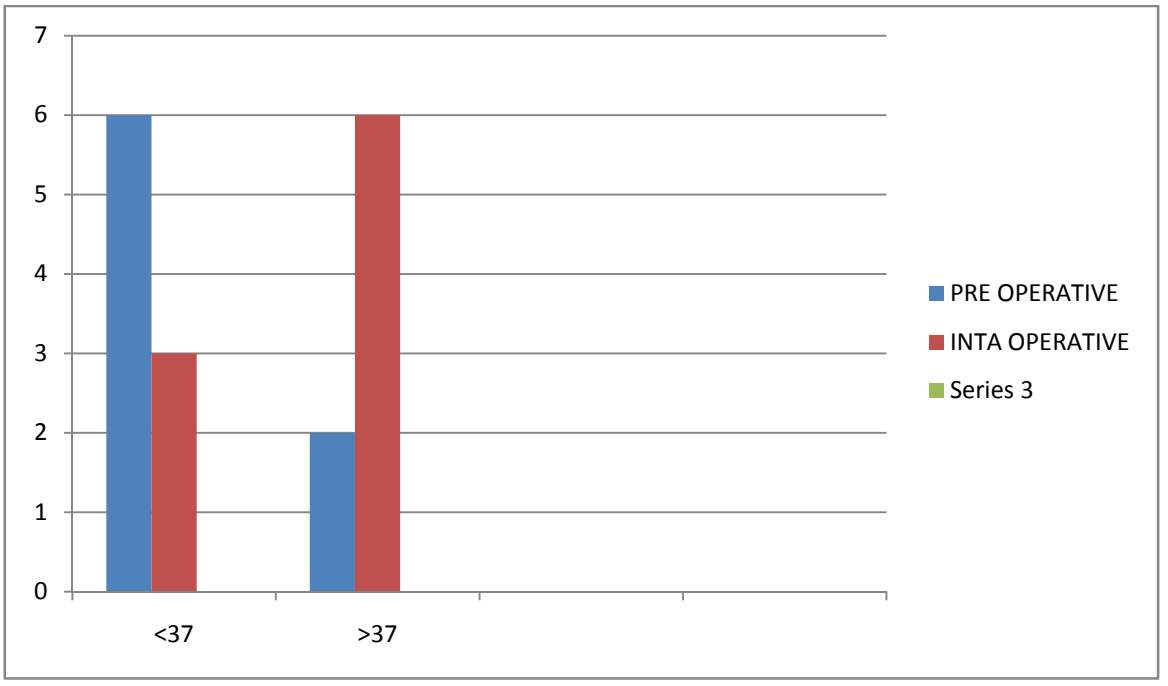
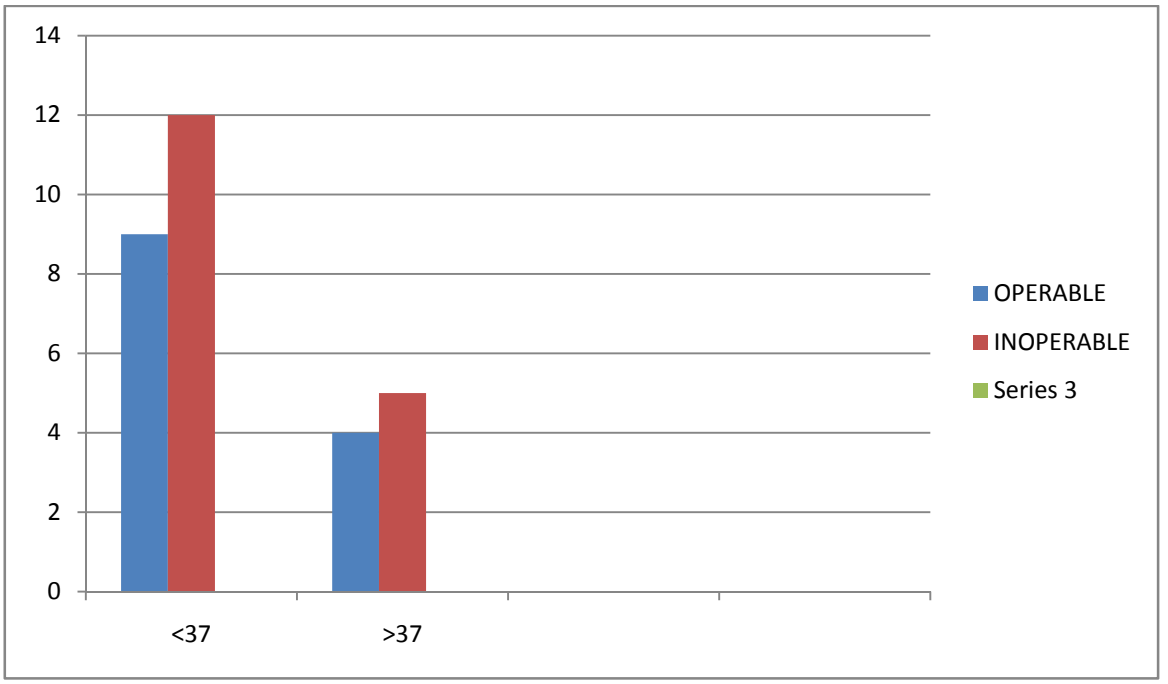


Table-6

CA 19-9	OPERABLE	INOPERABLE
<37	9 (70%)	12 (71%)
>37	4 (30%)	5 (29%)

CA 19-9 AMONG OPERABLE AND INOPERABLE CASES



DISCUSSION

DISCUSSION:

CA 19-9 as a tumor marker has been proven to be useful in predicting outcomes and in follow up of patients with carcinoma of head of pancreas. With lack of definitive evidence regarding the role of CA 19-9 in predicting operability in a case of carcinoma of the head of pancreas, I have chosen to analyse the same in a prospective study including 30 patients who underwent surgery for carcinoma of the head of pancreas, either curative or palliative.

In my study, it was observed that the incidence of pancreatic malignancies were almost equal in both males and females. Of the 30 cases 16 were males and 14 were females, and hence no gender preponderance noted.

Pancreatic malignancies continue to be a disease of the elderly, with 19 out of the 30 patients being in the age group of 51-70 years. There were 10 patients in the 51-60 group and 9 patients in the 61-70 years group.

As a part of the pre-operative evaluation Contrast enhanced CT (CECT) of abdomen and pelvis and serum CA 19-9 levels were done routinely. In the 30 patients with evidence of carcinoma of the head of pancreas included in the study, CA 19-9 levels were elevated in 9 patients

and were within normal limits in 21 patients. A cut-off of 37 IU/L was used.

When the 30 patients were taken up for surgery it was found that in 13 of the patients the malignancy was operable and they underwent classical Whipples pancreaticodudenectomy. In the other 17 patients the tumor was deemed inoperable and a palliative bypass procedure was done. Among the 17 patients who's tumor was inoperable,8 were diagnosed pre-operatively with CECT/MRCP, and the other 9 were found to be inoperable only during surgery.

Of the 13 patients who had operable tumors, CA 19-9 was elevated in 4 patients and was normal in the other 9 patients. Among the other 17 patients with inoperable tumors,CA 19-9 was elevated in 5 of the patients and was within normal limits in the other 12 patients.

Among inoperable cases 70% had raised CA-19-9 and among operable cases 30% showed raised CA 19-9. Hence CA 19-9 seems to be insignificant predictor of tumor resectability .

CONCLUSION

CONCLUSION:

- ✓ CA 19-9 as a tumor marker is a poor indicator of the extent of the disease and
- ✓ It is not a predictor of the resectability of the tumor in the head of pancreas.

LIMITATIONS OF THE PRESENT STUDY:

- ✓ The study includes data from the Dept of Surgery alone and does not include those surgeries done in the Institute of Surgical Gastro-Enterology. The same surgeries are done in the SGE dept too. So the results may not reflect the whole hospital's performance although the sample population is the same.
- ✓ A solely prospective study would have been much better than to rely on 2 years of retrospective data as done in this study.
- ✓ Some patients were lost on follow-up.

SIMILAR STUDIES

SIMILAR STUDIES:

Safi F, Schlosser W, Falkenreck S, Beger HG.

Prognostic value of CA 19-9 serum course in pancreatic cancer. Hepatogastroenterology. 1998;45:253-25

Schlieman MG, Ho HS, Bold RJ.

Utility of tumor markers

in determining resectability of pancreatic cancer. Arch Surg

2003; 138: 951-955; discussion 955-956

Kilic M, Gocmen E, Tez M, Ertan T, Keskek M, Koc M.

Value of preoperative serum CA 19-9 levels in predicting

resectability for pancreatic cancer. Can J Surg 2006; 49: 241-244

ABSTRACT

“THE ROLE OF CA 19-9 IN PREDICTING TUMOR RESECTABILITY IN CARCINOMA OF THE HEAD OF PANCREAS”

Background:

To study the role of CA 19-9 in predicting the resectability of the tumor in the head of pancreas .During the management of pancreatic carcinoma,CA 19-9 are measured to monitor response to chemotherapy and early detection of local recurrence.Nonetheless ,its exact role in the preoperative evaluation to assess the operability of the tumor is controversial.

Materials and Methods:

30 patients diagnosed with carcinoma of the head of pancreas on the basis of CECT/MRCP during the study period of 2 yrears are included in the study.During the preoperative evaluation of these patients ,CA 19-9 levels were measured and recorded.Patients who are medically unfit for surgery or those who did not warrant operative palliation are excluded from the study.After adequate preoperative preparation patients are taken up for surgery with either curative or palliative intent. During surgery the operative findings on the basis of which operability of the tumor is assessed, is documented and tabulated against corresponding values of CA 19-9.Then the diagnosis is confirmed based on the histopathological

report.The operative findings and its relation to the CA 19-9 levels are analysed and the results are interpreted.

Results:

Of the 30 patients who were operated, 13 patients had operable tumors and underwent WHIPPLES procedure and 17 of them had inoperable tumors and had to undergo palliative bypass procedures of some form.Of the 30 patients CA 19-9 levels were elevated in 9 patients and was normal in 21 patients.Among the 13 patients who had operable tumors, CA 19-9 was raised in 4 patients and was normal in 9 patients . Of the 17 patients who had inoperable tumors CA 19-9 was elevated in 5 patients and was normal in 12 patients.Among the 17 patients who had inoperable tumors,8 were diagnosed preoperatively,and of them CA 19-9 levels were raised in 2 patients and normal in 6 patients.In the group of 9 patients who had inoperable tumors diagnosed intraoperatively,CA 19-9 was raised in 4 of them and was normal in the remaining 5 of them.

Conclusions:

This study brings us to the conclusion that CA 19-9 ,as atumor marker has no role in predicting the tumor resectability in carcinoma of head of pancreas.

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BIBLIOGRAPHY

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APPENDIX

Proforma

Role of CA 19-9 in predicting tumor resectability in cancer head of pancreas

Investigator : **Dr.APARNA .M.J**, PGY3 – MS (Gen Surg)

Guide : **Prof. Dr. P. Darwin,** Chief, Unit S1

Name **:** **Age/Sex:**

I.P. No. **:**

Address **:**

Contact no **:**

D.O.A: **D.O.S :** **D.O.D:**

History and Physical:

Investigations:

HEMAT			**LFT**		
HB			T.BIL		
PCV			D.BIL		
RBC			AST		
TC			ALT		
DC			ALP		
PLT			T.PROTEIN		
ESR			S.ALB		
RBS FBS PPBS			P.T - T/C INR		
B.UREA			aPTT – T/C		
S.CREAT			S.CALCIUM		
S.Na+			CA 19-9		
S.K+			FOBT		
S.Cl-			**BL.GROUP**		
S.HCO3-					

X RAY	
USG	
CT/MRCP	
SCOPY	
HISTOPATH **(FNAC/BIOPSY)**	
OTHER	

OPINIONS:

PER OP DIAGNOSIS

OPERATIVE PROCEDURE

ANESTHESIA

FINDINGS

DRAINS

BLOOD LOSS

SPECIMEN FOR HPE

POST OP HPE REPORT

POST OP COURSE

Role of CA 19-9 in predicting tumor resectability in cancer head of pancreas

Investigator : **Dr.APARNA .M.J**, PGY3 – MS (Gen Surg)

Guide : **Prof. Dr. P. Darwin,** Chief, Unit S1.

Patient Information Module

You are being invited to be a subject in this study.

Before you participate in this study, I am giving you the following details about this trial, which includes the aims, methodology, intervention, possible side effects, if any and outcomes:

All patients diagnosed with cancer head of pancreas on the basis of CECT or MRCP will be included in this study. A detailed clinical history will be taken following a standardized proforma. A detailed clinical examination will be made and relevant investigations, basic and special investigations including CA 19-9 will be done.After complete evaluation,patients will be posted for surgery with either curative or palliative intent.During surgery a complete assessment of the extent and resectability of the tumour will be made and all the findings will be documented. If the tumour is resectable the resected specimen will be sent for HPE.In the event of only palliative bypass surgery any tissue sampling obtained during the surgery will be sent for the same.After histopathological confirmation of the diagnosis,the correlation between CA 19-9 and tumour respectability is analyzed.

The results arising from this study will be analyzed and used for academic purposes. You will be given clear instructions at every step and you are free to ask/ clarify any doubts. Your identity will remain confidential. You are free to withdraw from this trial at any point of time, without any prior notice &/ or without any medical or legal implications.

I request you to volunteer for this study.

Thanking You,

Investigator's Sign — Patient's Sign

(Dr. APARNA .M.J) — (Name:)

Role of CA 19-9 in predicting tumor resectability in cancer head of pancreas

Investigator : **Dr. APARNA M.J**, PGY3 – MS (Gen Surg)

Guide : **Prof. Dr. P. Darwin,** Chief, Unit S1.

Informed Consent

Name: Age/ Sex: IP:

I herewith declare that I have been explained in a language fully understood by me regarding the purpose of this study, methodology, proposed intervention, plausible side effects, if any and sequelae.

I have been given an opportunity to discuss my doubts and I have received the appropriate explanation.

I understand that my participation in this study is completely voluntary and that I am free to withdraw from this study at anytime without any prior notice &/ or without having my medical or legal rights affected.

I permit the author and the research team full access to all my records at any point, even if I have withdrawn from the study. However my identity will not be revealed to any third party or publication.

I herewith permit the author and the research team to use the results and conclusions arising from this study for any academic purpose, including but not limited to dissertation/ thesis or publication or presentation in any level.

Therefore, in my full conscience, I give consent to be included in the study and to undergo any investigation or any intervention therein.

Patient's Sign Investigator's Sign

(Dr. APARNA .M.J)

S.NO.	NAME	AGE/SEX	IP.NO.		CA 19-9	CECT/MRCP FINDINGS	CECT/MRCP FINDINGS				OPERATIVE FINDINGS	SURGERY DONE	HISTOPATHOLOGY REPORT
						MASS LESION	SMA ENMT.	SMPV INFILT.	LIVER METS	ASCITES			
1	ANDAL	65/F	43267		32	Present	-	-	-	-	Growth in the HOP without local spread/mets	WHIPPLES PROCEDURE	INFILTRATING ADENOCARCINOMA
2	MAHALAKSHMI	58/F	76140		30	Present	-	-	-	-	Growth in the HOP without local spread/mets	WHIPPLES PROCEDURE	INFILTRATING ADENOCARCINOMA
3	VARADAN	66/M	33410		765	Present	+	-	-	-	Growth in the HOP ,with infiltration into SMA	PALLIATIVE BYPASS	INFILTRATING ADENOCARCINOMA
4	MALAR	38/F	33954		24	Present	-	-	-	-	Growth in the HOP without local spread/mets	WHIPPLES PROCEDURE	INFILTRATING ADENOCARCINOMA
5	PONNAMMAL	53/F	10343		28	Present	-	+	-	-	Growth in the HOP,with infiltration of SMPV junction	PALLIATIVE BYPASS	INFILTRATING ADENOCARCINOMA
6	NAVEEN	52/M	32190		34	Present	-	-	+	+	Growth in the HOP,with multiple liver deposits,ascites	PALLIATIVE BYPASS	INFILTRATING ADENOCARCINOMA
7	MUPPIDATHI	36/F	41982		30	Present	-	-	-	-	Growth in the HOP without local spread/mets	WHIPPLES PROCEDURE	INFILTRATING ADENOCARCINOMA

8	THAHIRA	40/F	33501		25	Present	-	-	-	-	Lcally advanced growth infiltrating into portal vein	PALLIATIVE BYPASS	INFILTRATING ADENOCARCINOMA
9	RANGANAYAKI	35/F	11972		23	Present	-	+	-	-	Growth in the HOP,with infiltration of SMPV junction	PALLIATIVE BYPASS	INFILTRATING ADENOCARCINOMA
10	LAKSHMI	55/F	12844		23	Present	-	-	-	-	Locally advanced growth with peritoneal,liver deposits	PALLIATIVE BYPASS	INFILTRATING ADENOCARCINOMA
11	IRULAPPAN	80/M	15593		17	Present	-	-	-	-	Growth in the HOP without local spread/mets	WHIPPLES PROCEDURE	INFILTRATING ADENOCARCINOMA
12	ELAMMAL	65/F	17601		234	Present	-	-	-	-	Growth in the HOP with infiltration into SMA,SMV	PALLIATIVE BYPASS	INFILTRATING ADENOCARCINOMA
13	VARADHAN	65/M	28886		36	Present	-	-	-	-	Locally advanced growth with peritoneal,liver deposits	PALLIATIVE BYPASS	INFILTRATING ADENOCARCINOMA
14	SAIT	32/M	24535		19	Present	-	-	-	-	Growth in the HOP,with direct infiltration of SMPV jn.	PALLIATIVE BYPASS	INFILTRATING ADENOCARCINOMA
15	SHAKUNTHALA	60/F	24549		974	Present	-	-	-	-	Growth in the HOP without local spread/mets	WHIPPLES PROCEDURE	INFILTRATING ADENOCARCINOMA

16	BASKAR	65/M	26687		26	Present	-	-	-	-	locally infiltrated growth with fixity to SMA,SMV	PALLIATIVE BYPASS	INFILTRATING ADENOCARCINOMA
17	MUGUNTHAN	44/M	30093		12000	Present	-	-	-	-	Growth in the HOP without local spread/mets	WHIPPLES PROCEDURE	INFILTRATING ADENOCARCINOMA
18	YASODAMMAL	60/F	32807		22	Present	-	-	-	-	Locally advanced growth with peritoneal,liver deposits	PALLIATIVE BYPASS	INFILTRATING ADENOCARCINOMA
19	GANAPATHY	51/M	13329		29	Present	-	-	+	+	Growth in the HOP, with extensive liver mets,ascites	PALLIATIVE BYPASS	INFILTRATING ADENOCARCINOMA
20	GNANAKRISHNAN	46/M	39220		834	Present	-	-	-	-	Growth in HOP,with involvement upto porta hepatis	PALLIATIVE BYPASS	INFILTRATING ADENOCARCINOMA
21	NITHYA	47/F	39122		16	Present	-	-	-	-	Growth in the HOP without local spread/mets	WHIPPLES PROCEDURE	INFILTRATING ADENOCARCINOMA
22	MUNIYAPPAN	60/M	36739		50000	Present	-	-	-	-	Growth in the HOP without local spread/mets	WHIPPLES PROCEDURE	INFILTRATING ADENOCARCINOMA
23	SADAIYYAN	54/M	19669		37	Present	-	-	-	-	Growth in the HOP without local	WHIPPLES PROCEDURE	INFILTRATING ADENOCARCINOMA

											spread/mets		
24	THANIGAIVELU	65/M	36779		24	Present	-	-	-	-	Growth in the HOP with extensive infiltration of PV	PALLIATIVE BYPASS	INFILTRATING ADENOCARCINOMA
25	CHANDRABABU	67/M	29011		28	Present	-	-	+	+	Growth in the HOP with deposits in liver,peritoneum	PALLIATIVE BYPASS	INFILTRATING ADENOCARCINOMA
26	SADAYAMMAL	38/F	28044		26	Present	-	-	-	-	Growth in the HOP without local spread/mets	WHIPPLES PROCEDURE	INFILTRATING ADENOCARCINOMA
27	MUNUSAMY	64/M	25679		2567	Present	-	-	-	-	Growth in the HOP without local spread/mets	WHIPPLES PROCEDURE	INFILTRATING ADENOCARCINOMA
28	PAPPANAIDU	59/M	15673		18	Present	+	-	-	-	Growth in the HOP,with encasement of SMA,ascites	PALLIATIVE BYPASS	INFILTRATING ADENOCARCINOMA
29	PENICILAIYYA	62/M	36789		7643	Present	-	+	-	-	Growth in the HOP,with infiltration of SMPV junction	PALLIATIVE BYPASS	INFILTRATING ADENOCARCINOMA
30	DEVAKI	43/F	16578		432	Present	-	-	-	-	Growth in the HOP without local spread/mets	WHIPPLES PROCEDURE	INFILTRATING ADENOCARCINOMA